ABSENT CIRCULATORY REFLEXES IN DIABETIC NEURITIS

E. P. SHARPEY-SCHAFER
F.R.C.P.
PROFESSOR OF MEDICINE

P. J. TAYLOR
M.B., B.Sc. Lond., M.R.C.P.
MEDICAL REGISTRAR

From the Department of Medicine, St. Thomas's Hospital, London, S.E.1

IN fully developed tabes dorsalis circulatory reflexes have been shown to be absent (Sharpey-Schafer 1956b). Thus an acute decrease in arterial pulse pressure, produced by the erect posture or the Valsalva manœuvre, did not result in normal reflex constriction, while an increase of pulse pressure on squatting, or imposed cough transients, did not cause normal vasodilatation. The lesion appeared to lie on the afferent reflex pathway, since the efferent vasomotor nerves were intact.

Such a circulation acts largely mechanically; and as heart-rate changes are also abolished, mean arterial pressure bears an approximately linear relationship to the stroke output of the heart. The value of this simple mechanical circulation to circulatory, endocrine, and other workers is considerable in the study of complex normal changes. Tabes dorsalis, however, is becoming rare in this country and seems virtually to have disappeared in America, but it is likely that other neurological diseases might show the same phenomena. It is now known that this is so and a considerable variety of common and rare diseases are associated with absent baroceptor reflexes. One of the commoner conditions, diabetic neuritis, is described in this paper.

Material and Methods

337 consecutive patients attending a diabetic clinic were examined for evidence of neuropathy. Diminished or absent ankle-jerks, loss of sensation to pinprick, and diminished or delayed deep pain sense were the main physical signs sought.

The Valsalva manœuvre was used to test circulatory reflexes. This procedure is the simplest method of producing great changes in the circulation, the decrease in stroke output and pulse pressure and the consequent vasoconstriction being easily detected. By feeling the pulse it is possible to be certain that the response to a Valsalva manœuvre is normal (Sharpey-Schafer 1955). Doubt may arise from lack of rate change in elderly subjects or various artefacts such as poor blowing. Those patients whose response was not obviously normal were investigated further. The tests were similar to those used on tabetics (Sharpey-Schafer 1956b). Continuous arterial pressures were recorded with capacitance manometers and limb blood-flow by plethysmography. The effects of the Valsalva manœuvre, tipping into the erect posture, coughing, mental arithmetic, hyperventilation, and carotid-sinus pressure were recorded.

The efferent vasomotor pathway was studied in 3 patients by the effect on hand blood-flow of indirect heating and a sudden deep inspiration.

Results

268 of the 337 diabetic patients studied had normal circulatory reflexes. The remaining 69 had some evidence of neuropathy and an abnormal response to the Valsalva manœuvre. 35 of these were studied fully. Since some cases were not investigated, figures of incidence can only be minimal. Of the 35 investigated 17 showed complete absence of effective circulatory reflexes and 14 diminution of response when compared with a large group of normal persons.

Evidence for Absent Circulatory Reflexes

The results were similar to those obtained in tabetics. On performing the Valsalva manœuvre the most conspicuous finding in continuous arterial records was absence of the overshoot, which in the normal is caused by reflex constriction (fig. 1). There is one point here which needs stressing: it is essential for the period of raised intrathoracic pressure to be sufficiently prolonged for the maximum pulse pressure decrease to last at least 5–7 seconds. This is the time period needed for the system

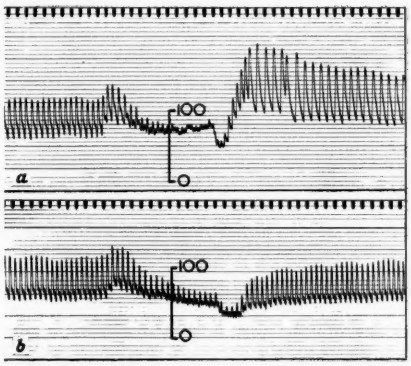

Fig. 1—Continuous arterial records showing effects of Valsalva manœuvre (time marker in sec., calibration in mm. Hg in this and subsequent records): *a*, normal reflex constriction in a diabetic of 34 years' standing; *b*, case 2, showing absence of reflex constriction. After release of the high intrathoracic pressure, pulse pressure and diastolic pressure do not regain control level for more than 15 sec.

to respond to an acute diminution in afferent impulses (Sharpey-Schafer 1956a, Howarth and Sharpey-Schafer 1957). The normal rise of mean pressure during blowing, which signals the onset of vasoconstriction, was also absent, as were the normal acceleration of heart-rate with diminishing stroke output and the conspicuous slowing at the height of the overshoot. The behaviour of the circulation on release of the high intrathoracic pressure showed important changes. In the normal a pulse pressure greater than control level is reached in about 5 sec., even in fully atropinised subjects without rate change. When circulatory reflexes are absent and the circulation acting mechanically, the stroke output and arterial pulse pressure only increase slowly over 15 or more seconds to reach control value. The explanation of

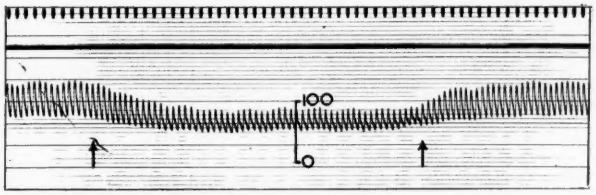

Fig. 2—Diabetic with absent circulatory reflexes.

At the first arrow the patient is tipped into the erect posture and at the second arrow is returned to the supine position. The circulation is acting purely mechanically, and mean arterial pressure is related to the stroke output.

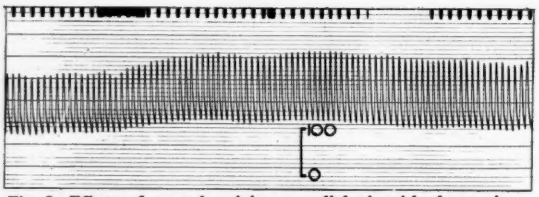

Fig. 3—Effects of mental activity on a diabetic with absent circulatory reflexes.

At the black signal on the time marker the patient was asked to do simple mental arithmetic. Mean pressure and pulse pressure increase and there is a slight increase in heart-rate. Mean pressure remains elevated for many seconds. In the normal the same initial response causes reflex dilatation and return of arterial pressure towards control level in a few seconds.

this effect probably lies in the behaviour of the venous system, and evidence on this point will be presented elsewhere.

The effects of tipping into the erect posture were identical with those obtained in tabetics (fig. 2). There was no evidence of reflex constriction, and the fall of mean arterial pressure in the erect posture reflected the change in stroke output. As in tabetics there was no rate change. The effects of large cough transients, hyperventilation, and mathematical problems were also identical with those found in tabetics; fig. 3 shows an example of the behaviour of these mechanical circulations without reflexes. The effects of squatting and standing running were not investigated.

The Efferent Vasomotor Pathway

3 diabetic patients who showed absence of circulatory reflexes with the tests described above were further studied to demonstrate the continuity of the efferent vasomotor pathway. Two methods were used. The first was indirect heating, causing vasodilatation of the vessels of the hand through the central nervous system and thence via the efferent sympathetic nerves. An afferent nervous pathway is not involved (the small "immediate" effect to strong heating of the trunk area, described by Kerslake and Cooper [1950], was not investigated). The second method was a sudden deep inspiration, causing constriction in hand vessels (Bolton et al. 1936) by a spinal reflex mechanism (Gilliatt et al. 1948) with an efferent pathway via the vasomotor nerves.

The effects of these procedures, shown in fig. 4, were obtained in all 3 diabetics. These results are similar to those in normal persons and tabetics and indicate that the efferent vasomotor pathway is intact. Of the 3 heated diabetics 2 showed extensive sweating, and although patchy loss of sweating areas is known in diabetic neuropathy the evidence suggests that the lesion causing loss of circulatory reflexes lies, as in tabes, on the afferent pathway.

Partial Defects of Circulatory Reflexes

14 patients showed a response to the Valsalva manœuvre which lay between the normal limits and complete absence of circulatory reflexes (fig. 5). In tabes dorsalis such cases are also known and 9 have been recorded, the neurological signs being limited to absent ankle-jerks,

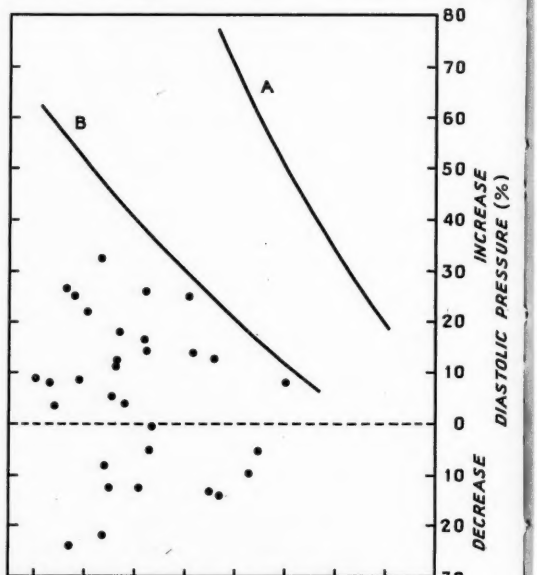

Fig. 5—Reflex responses of all diabetic patients shown in table, with percentage decrease of pulse pressure during Valsalva manœuvre plotted against percentage increase in diastolic pressure at the height of the overshoot (Sharpey-Schafer 1955). Lines A and B represent the upper and lower limits of 350 normal persons.

Some points fall below the abscissa since diastolic change was calculated about 5 sec. after release of the high intrathoracic pressure, and at this time, in some patients, diastolic pressure has not regained control level. (See fig. 1 and text.)

sensory loss in the legs, and pupillary changes. Fully developed tabes continues to show complete absence of circulatory reflexes, and 12 further cases can be added to the 11 originally described (Sharpey-Schafer 1956b).

Associated Neurological and Circulatory Findings

The results are shown in the table. Many patients in the clinic had had severe diabetes for many years, and yet had normal circulatory reflexes. The severity and duration of the disease, therefore, do not seem to be necessary factors for involvement of this part of the nervous system. Although ankle-jerks were absent or diminished in every case, knee-jerks were often present when circulatory reflexes were absent. Changes in pain sense varied from slight diminution in the feet to extensive

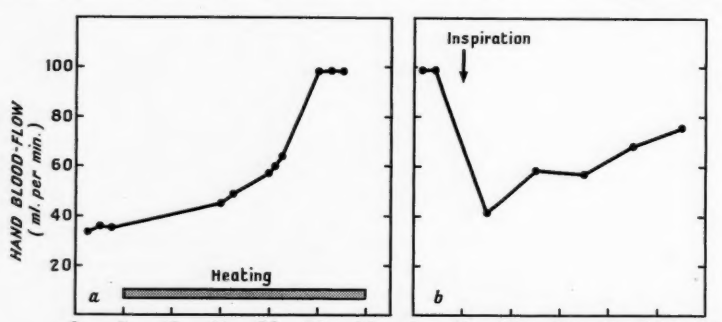

Fig. 4—*a*, effect of heating the legs and left arm on blood-flow in the right hand in a diabetic with absent circulatory reflexes; *b*, effect of a single deep inspiration on hand blood-flow in a similar patient, showing normal response.

loss over legs and trunk. Impotence, which is common in autonomic disorders, was present in 9 of 10 patients without circulatory reflexes. The remaining patients were not questioned. These findings suggest that small-fibre pathways may be first affected in diabetic neuritis; and that defects of circulatory reflexes can develop with very slight neurological signs..

The supine arterial pressures shown in the table might be regarded as showing hypertension in a number of the patients. The use of the term "hypertension" is a question of definition, and even when intra-arterial records are available and cuff artefacts and physiological variations are eliminated it is difficult to know where the normal ends and hypertension begins. It is unlikely, however, that higher levels of arterial pressure in some of these patients are due to absence of afferent baroceptor impulses—a mechanism which has been suggested as a cause of "essential hypertension" and which experiment shows to be incorrect. The table shows that some patients without circulatory reflexes have normal arterial pressures. A very similar distribution of resting supine arterial pressures is seen in tabes.

Postural Hypertension and Syncope

1 patient showed severe postural hypotension. For some weeks he was liable to lose consciousness while standing still in the erect posture, the mean arterial pressure falling to 40 mm. Hg or less. Even when supine, consciousness was lost during the Valsalva manœuvre when effective supply pressure (arterial minus venous pressure) across the brain fell to similar levels.

2 other patients had a similar fall of arterial pressure and syncope when performing the Valsalva manœuvre in the erect posture—a relatively more violent method than postural change of reducing cardiac filling pressure and stroke output.

DIABETIC PATIENTS WITH ABSENT CIRCULATORY REFLEXES

Case no.	Age (yr.)	Sex	Duration of diabetes (yr.)	Severity of diabetes	Ankle and knee jerks present	Sensory loss	Supine B.P. (mm. Hg)	Remarks
1	66	M	8	++	O	+++	196/80	..
2	66	M	<1	++	O	+++	136/82	Impotent; postural syncope
3	57	M	6	++	K	++	209/105	Impotent
4	51	M	8	++	O	++	152/67	Impotent
5	53	M	20	++	K	++	211/92	Impotent
6	61	M	6	++	KA	++	188/89	..
7	57	M	16	++	K	+	219/108	..
8	43	M	<1	++	K	++	152/78	Impotent
9	55	M	7	++	K	++	159/74	Impotent
10	53	M	37	++	KA	+	192/92	Not impotent
11	56	M	22	++	K	++	145/72	..
12	69	M	1	+++	O	+++	122/54	..
13	62	M	<1	++	K	++	166/72	..
14	74	M	8	+++	O	+++	221/100	..
15	57	M	2	+++	K	+++	164/73	..
16	60	M	<1	+	K	+	162/81	..
17	58	F	10	++	O	++	200/98	..
18	45	M	21	++	O	++	116/60	..
19	42	M	3	+++	KA	+	140/85	..
20	40	M	12	++	K	++	192/96	Impotent
21	62	M	20	++	K	++	138/62	Impotent
22	48	M	1	++	O	+	150/77	..
23	74	M	5	++	K	+++	178/85	Impotent
24	60	M	3	+	K	+	132/77	..
25	51	M	27	++	K	++	163/78	..
26	63	M	1	+++	KA	+	121/63	..
27	56	F	23	++	K	+	178/100	..
28	63	F	9	++	K	+	188/79	..
29	45	F	23	++	O	+++	164/77	..
30	72	F	6	+	K	+++	260/125	..
31	52	F	21	++	O	+	182/86	..

Severity of diabetes: + = hyperglycæmia, no insulin. ++ = controlled on moderate doses of insulin. +++ = frequent ketosis.
Tendon jerks: O = knee and ankle absent. K = knee present, ankle absent. KA = knee and ankle present.
Sensory loss to pinprick: + = over feet. ++ = over legs. +++ = over legs and trunk.
Arterial pressure: taken from intra-arterial record.
Cases 18–31 had a partial defect of circulatory reflexes.

Discussion

The results show that not only patients with tabes dorsalis but also many diabetics are without circulatory reflexes. The effect of this functional defect on the prognosis of diabetic patients can be good or bad. Postural syncope is the most obvious disadvantage; but, as in tabes, our results show that this is rare. Isolated cases have been recorded.

Thus Ellis and Haynes (1936) probably described such a case, for 1 of their patients with postural syncope of unknown ætiology was a "diabetic fully controlled by insulin". Burnum et al. (1954), on the other hand, published a typical continuous arterial record of the Valsalva manœuvre without reflex responses in a diabetic with postural hypotension. Odel et al. (1955), using the cuff method, claimed to have found 16 cases of postural hypotension in diabetics; 1 patient had syncope in the erect posture. They deduced that the lesion lay on the efferent sympathetic pathway, but their methods and reasoning are open to criticism.

With an acute fall of arterial pressure and syncope the patient may become wedged in the erect or sitting position. Straining at stool, a Valsalva manœuvre, in a small locked lavatory is perhaps the commonest situation to be avoided. Death has been known to occur, and pathologists would normally find no cause.

Drugs which dilate the venous system, block sympathetic ganglia, or otherwise interfere with the central or efferent pathways of circulatory reflexes can produce disastrous hypotension in such patients. Since mean arterial pressure is a function of the stroke output of the heart, surgical operations, with the combined effect of anæsthetic drugs and hæmorrhage, should not be undertaken without realising the necessity of maintaining cardiac filling pressure by transfusion. The "diabetic abdomen", with acute pain simulating an abdominal catastrophe, may indicate the involvement of sensory nerves similar in calibre to circulatory afferents. In the past, 3 such cases have been seen in which the abdomen was unhappily opened. There were no abnormal post-mortem findings.

On the other hand possible advantages are considerable. Those diabetics with peripheral arterial disease may at least be free from reflex constriction under ordinary conditions of living. In heart-failure, too, there is evidence that the changes producing clinical congestive failure are largely reflex in origin. Absent circulatory reflexes might well protect against one of the vicious-circle mechanisms of acute left-heart failure: rise of venous pressure—reflex venous constriction—further rise of venous pressure.

Increased production of aldosterone is thought to be mediated through diminished afferent baroceptor impulses and an efferent hormonal mechanism (Bartter et al. 1959). Ganglion-blocking agents do not interrupt this pathway, but possibly tabes and diabetes may. Similarly afferent impulses from the heart may be one of the factors governing water-salt excretion by the kidney. While these relatively slow homœostatic mechanisms can well have been advantageous to youthful primitive man, they may not be so useful to his ageing civilised descendants.

Apart from extensive surgery, disease of the nervous system is the only known method of interrupting these afferent pathways. No-one would suggest that tabes or diabetes should be acquired deliberately, but sufferers from these diseases can take comfort that they are not totally without assets.

Summary

Circulatory reflexes were studied by continuous arterial records, using the Valsalva manœuvre, tipping, coughing,

hyperventilation, and mental arithmetic to change the stroke output of the heart.

Of 337 diabetic patients 17 had absent circulatory reflexes and 14 a partial defect of the reflex system.

The effects of indirect heating and a sudden deep inspiration on hand blood-flow were normal, indicating that the defect lay on the afferent pathway.

Of other neurological lesions, impotence in males showed the best correlation with absent circulatory reflexes. Severity and duration of the diabetic state were not factors.

1 patient had postural syncope, and in 2 others arterial pressure reached syncopal levels with more severe procedures.

The patients formed part of the clinical material of a large diabetic clinic under the care of Dr. H. K. Goadby, to whom we are much indebted.

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CEREBRAL ANGIOGRAPHY IN THE DIAGNOSIS OF THE ACUTE STROKE

J. W. D. BULL
M.A., M.D. Cantab., F.R.C.P., F.F.R.
RADIOLOGIST

JOHN MARSHALL
M.D. Manc., F.R.C.P.E., M.R.C.P., D.P.M.
READER IN CLINICAL NEUROLOGY

D. A. SHAW
M.B. Edin., M.R.C.P.E.
LECTURER IN CLINICAL NEUROLOGY

From the Lysholm Radiological Department and the Academic Unit in Neurology, The National Hospital and Institute of Neurology, Queen Square, London, W.C.1

As specific methods of treating the patient with an acute stroke have evolved greater accuracy in diagnosing the cause of this syndrome has become desirable. Anticoagulant therapy (Fisher 1958, Carter 1959), the surgical evacuation of intracerebral hæmatomas (McKissock et al. 1959), and the relief of carotid occlusion in the neck (Rob and Wheeler 1957), all demand a precision in diagnosis which is unattainable by clinical means alone.

Aring and Merritt (1935) made a retrospective survey of the signs and symptoms in a series of patients with strokes in whom the cause was revealed at necropsy, but careful application of their diagnostic criteria does not enable one to distinguish confidently even between intracerebral hæmorrhage and cerebral infarction. For example, Dalsgaard-Nielsen (1956) found that the clinical diagnosis of cerebral hæmorrhage in 239 cases was confirmed at necropsy in only 155 (65%), and that the diagnosis of cerebral arterial thromboembolic occlusion in 139 cases was confirmed in only 81 (58%).

Ancillary methods of diagnosis are therefore of great importance.

Although the value of cerebral angiography in diagnosing intracranial aneurysms, cerebral arteriovenous malformations, and subdural and extradural hæmatomas, is beyond doubt, it has been less extensively studied in cerebral arterial occlusion and intracerebral hæmorrhage, which are commoner. A recognised use of angiography is to exclude tumours, and particularly subdural hæmatomas, which may present clinically as strokes (Bull 1958). In addition, various workers have reported selected examples in which angiography revealed a lesion which was sometimes unsuspected clinically and sometimes amenable to therapy (Livingston et al. 1955, Feiring and Sussman 1956, Balkissoon et al. 1959, Frantzen et al. 1959, Keirns and Whiteleather 1959, Kuhn 1959). But the value of angiography in relation to the acute stroke has not been properly assessed.

We undertook this study to assess the contribution of angiography in diagnosing the site and pathology of lesions which give rise to an acute stroke.

The Study

Our series comprised 80 consecutive patients who were admitted to the Academic Unit of the National Hospital, Queen Square, and submitted to cerebral angiography within seventy-two hours of the onset of an acute stroke.

The term acute stroke was taken to include all major disturbances of cerebral function which, on clinical grounds, were attributed to a vascular lesion in the carotid or vertebrobasilar territory, other than aneurysm, arteriovenous malformation, or subdural or extradural hæmatoma. Several cases referred as "strokes" did not fulfil these criteria, and were not included in the series. The upper age-limit of patients admitted to the study was seventy. No other criteria of selection were employed. The fact that the patients were admitted to a neurological unit does not mean that they presented as problems of neurological diagnosis. The majority were referred by the Emergency Bed Service from among cases of stroke offered by general practitioners.

5 patients were in the fourth decade, 21 in the fifth, 38 in the sixth, and 16 in the seventh. There were 41 men and 39 women. Such history as was available was taken from the patient or relatives, and the patient was examined fully. The cerebrospinal fluid was scrutinised for blood by the naked eye and microscopically, and plain radiographs of the skull were taken. When the site and nature of the lesion had been diagnosed clinically the patient was submitted to angiography. The vascular territory supplied by one major vessel (common carotid or vertebral) only was examined, the appropriate vessel being chosen on the basis of the clinical diagnosis. We appreciated that the investigation of only one vessel might be inadequate in some cases, but this policy was necessary because all the patients were to be included in a controlled therapeutic trial which demanded uniformity in the preliminary investigations.

Results

The radiological diagnoses based on the angiographic examinations in this series are shown in table I. In 33 of the 80 cases (41%) the angiogram showed a lesion, in 46 no abnormality was detected, and 1 vertebral angiogram was unsuccessful.

TABLE I—ANGIOGRAPHIC FINDINGS IN 80 CONSECUTIVE CASES OF STROKE

Angiographic findings	No. of cases
No abnormality detected:	
Carotid	45
Vertebral	1
Internal-carotid occlusion:	
Complete	10
Partial	4
Middle-cerebral occlusion	8
Anterior-cerebral occlusion	2
Basilar occlusion	2
Hæmorrhage:	
Intracerebral	6
Intracerebral (aneurysm shown)	1
Failed vertebral angiogram	1
Total	80

TABLE II—CORRELATION BETWEEN ANGIOGRAPHIC AND CLINICAL DIAGNOSES

Clinical diagnoses	Angiographic diagnoses								Total clinical diagnoses
	No abnormality detected	Internal-carotid occlusion	Middle-cerebral occlusion	Anterior-cerebral occlusion	Basilar occlusion	Intracerebral hæmorrhage	Hæmorrhage (aneurysm shown)	Failed vertebral angiogram	
Internal-carotid occlusion	**6**	**4**	**1**	..	..	..	..	..	11
Middle-cerebral occlusion	27	6	**2**	..	..	2	..	..	37
Anterior-cerebral occlusion	2	..	..	**2**	..	..	..	..	4
Basilar occlusion	1	..	..	..	**2**	..	..	1	4
Intracerebral hæmorrhage	9	2	3	..	..	**4**	1	..	19
Middle-cerebral embolus	1	2	**2**	..	..	..	..	..	5
Total angiographic diagnoses	46	14	8	2	2	6	1	1	80

The figures in heavy type indicate that the diagnosis was made both angiographically and clinically.

The most striking finding, and potentially the most important from the therapeutic standpoint, was that in 14 cases occlusion of the internal carotid artery was demonstrated (10 complete and 4 partial). Only 4 of these cases had been diagnosed clinically (table II) although, throughout the study, the clinicians were fully aware of the possibility of internal-carotid occlusion and this diagnosis was preferred to that of middle-cerebral-artery occlusion in doubtful cases. Thus the absence of carotid-artery pulsation in the neck, or the presence of a bruit, were constantly sought, and any patient with recurrent transient strokes was diagnosed clinically as having carotid occlusion.

8 patients had occlusion of the middle cerebral artery, all at the classical site just proximal to the bifurcation or trifurcation of the main vessel. The angiographic diagnosis of middle-cerebral-artery occlusion was infrequent in relation to the clinical diagnosis, which was made in 37 patients. There are several reasons for this discrepancy.

1. Angiography is a relatively crude procedure, and occlusion of the larger vessels only can be diagnosed with certainty. The number of main branches arising from the middle cerebral artery varies; hence the absence of a vessel shadow does not necessarily indicate occlusion. Moreover the smaller vessels, such as those supplying the internal capsule, occlusion of which can produce severe clinical deficits, are beyond the scope of current angiographic technique.

2. No account was taken in our study of minor changes, such as variations in the calibre of vessels and irregularity of their walls, which are of diagnostic value in cerebrovascular disease (Bull, Couch, Joyce, Marshall, Potts, and Shaw 1960).

3. We did not attempt to demonstrate the points of origin of the carotid and vertebral arteries which may be narrowed by atherosclerosis.

But the angiographic diagnosis of 8 cases of middle-cerebral occlusion was of value, for 3 of these had been diagnosed clinically as cerebral hæmorrhage, and 1 as internal-carotid occlusion.

Failure of the anterior cerebral artery to fill with contrast medium may be due to an anatomical anomaly of the circle of Willis, the blood-supply being derived from the opposite side. Hence, unless bilateral carotid angiograms are performed, proximal occlusion of the anterior cerebral artery cannot be diagnosed confidently unless it is distal to the anterior communicating artery. In this series, because both anterior-cerebral-artery occlusions were well distal to the anterior communicating artery, the diagnosis was made on unilateral carotid angiography. In 1 case the finding was confirmed postmortem.

Angiography revealed occlusion of the basilar artery in 2 cases, in both paradoxically by the carotid route. 4 cases were diagnosed clinically, and 2 of them were submitted to vertebral angiography; one angiogram was normal, and one was a failure. In the other 2 patients, a lesion in the territory of the basilar artery was diagnosed primarily, but the possibility of a hemisphere lesion was also considered. We were, rightly or wrongly, somewhat nervous of vertebral angiography in patients with an acute stroke. Hence carotid angiograms were performed in these 2 cases, and they showed retrograde filling of the distal part of the basilar artery, which can only occur if the normal blood-flow through the artery is obstructed or reduced.

Intracerebral hæmorrhage was diagnosed angiographically in 6 cases, of which only 4 had been diagnosed clinically. In 1 further case the angiogram showed that hæmorrhage had arisen from a ruptured aneurysm, a finding which was surprisingly uncommon in our series. We tried to exclude aneurysms and arteriovenous malformations from the series, but some 25% of cerebral aneurysms rupture into the cerebrum, ventricles, or subdural space as well as into the subarachnoid space (McKissock and Walsh 1956) and so may present as strokes. The angiographic diagnosis of intracerebral hæmorrhage is based on displacement of vessels, though this may in fact be due to any space-occupying lesion. The angiographic appearances of a subdural hæmatoma are distinctive, and a pathological circulation within some tumours may indicate their nature; but in most cases one can only decide that a space-occupying lesion is due to intracerebral hæmorrhage by inference from the clinical story. In the presence of a stroke, cerebral vessels may also be displaced by œdema consequent upon cerebral infarction, which, unless occlusion of an artery is revealed, cannot be distinguished from displacement due to hæmorrhage.

Table I shows the results of a single angiogram performed within seventy-two hours of the onset of the stroke. But, because the clinical picture in such patients is not static, further angiograms may be indicated later and may provide more information. This is illustrated by 2 cases from this series.

CASE 1 had two transient, right-sided strokes, followed by a third which left him with a right hemiparesis. At this time a left carotid angiogram showed no abnormality. He had two more right-sided strokes, after which the left carotid angiogram was repeated, showing occlusion of the middle cerebral artery. After sixth and seventh right-sided strokes, a third left carotid angiogram showed occlusion of the left anterior cerebral artery as well as the previous middle-cerebral occlusion.

CASE 2 underwent left carotid angiography, which revealed no abnormality, at the onset of a right hemiplegia. His hemiplegia improved at first, but later deteriorated. A second angiogram, seven weeks after the first, showed a tumour circulation in the parietal region, with appropriate displacement of the main vessels which had been normally placed in the initial angiogram. Biopsy revealed an astrocytoma, grade III, but review of the first angiogram failed to disclose any abnormality.

Another patient, who had had a radical mastectomy for carcinoma of the breast, was diagnosed clinically as having a middle-cerebral occlusion because of the mode of onset and subsequent improvement of her stroke. Carotid angiography showed no abnormality. She was discharged from hospital well, but returned fourteen

weeks later with the clinical picture of raised intracranial pressure. Ventriculography revealed a metastatic tumour, which was confirmed at biopsy.

Neuroradiologists and clinicians know well that rapidly growing neoplasms may not manifest themselves at an initial angiographic or pneumographic study, although a few weeks or months later they may become obvious. As the patients in our series have been followed for at least six months, other misdiagnoses are unlikely.

Taking the figures as a whole, 16 of the 33 positive angiograms confirmed the clinical diagnosis, while 17 showed it to be incorrect. Thus in 17 of the 80 cases (21%) angiography was an essential adjunct to diagnosis; and this figure is important when definitive treatment, such as anticoagulant therapy, thromboendarterectomy, or surgical evacuation of a hæmatoma is contemplated. Furthermore, in assessing the value of angiography, one must take into account those cases where a clinical diagnosis which might have led to definitive treatment was refuted. For example, internal-carotid occlusion was diagnosed clinically in 11 cases but confirmed angiographically in only 4. Likewise, middle-cerebral (non-embolic) occlusion was diagnosed clinically in 37 cases but confirmed only twice; this would be important were it decided to give anticoagulant therapy only to patients with indisputable evidence of an occlusive lesion. In 5 cases where the clinician diagnosed embolic occlusion of the middle cerebral artery, this was shown angiographically in 2.

Complications

Cerebral angiography is not without hazard, perhaps especially in patients with cerebral atherosclerosis. In our series the clinical picture became worse after the angiogram in 9 cases. The exacerbations included increase in the severity of hemiparesis, hemianæsthesia, dysphasia, and hemianopia, although, fortunately, they were all transient. In 7 of these patients no abnormality was detected in the angiogram; 6 were diagnosed clinically as middle-cerebral occlusions, and 1 as basilar occlusion. In 1 case angiography confirmed the clinical diagnosis of anterior-cerebral occlusion, and in the other the diagnosis of internal-carotid occlusion. The criterion determining the complication-rate was very strict, for any increase in the clinical deficit within twenty-four hours of angiography was regarded as a complication. As the clinical condition of some patients was deteriorating before angiography, the complication-rate of 11% may well overestimate the hazard.

Necropsy Findings

21 patients of the series died, and 19 were examined post mortem (Prof. W. Blackwood and Dr. W. G. P. Mair). Table III correlates the angiographic, clinical, and postmortem diagnoses, revealing the very important fact that of the 12 cases of cerebral hæmorrhage only 4 were diagnosed angiographically. 8 of them were diagnosed clinically, but 3 were diagnosed neither clinically nor angiographically. 2 of these 3 patients had no blood in the cerebrospinal fluid, and the 3rd had blood which was thought to be traumatic. But it may be that the hæmorrhages were small when the clinical and angiographic examinations were made, but increased in size by the time the patient died. Of the vascular occlusions 2 were in the internal carotid artery, and it is worth noting that neither was diagnosed clinically, though both were seen in the angiogram.

TABLE III—ANGIOGRAPHIC DIAGNOSES IN RELATION TO NECROPSY FINDINGS

Angiographic diagnoses	No. of cases	Necropsy findings	
		Cases of hæmorrhage	Cases of vascular occlusion
No abnormality	8	7	1
Cerebral hæmorrhage ..	4	4	..
Vascular occlusion	7	1	6

Discussion

The value of angiography has to be assessed in relation to the clinical problem with which help is sought. We would emphasise again that our series comprised typical strokes as commonly seen in general medical practice, with no preselection other than an upper age-limit of seventy. Our study has shown that, in such an unselected series, cerebral angiography can aid the diagnosis of the site and pathology of lesions which cause acute strokes. This is apart from its undoubted function of excluding lesions such as aneurysms, arteriovenous malformations, subdural hæmatomas, and tumours which may present as strokes.

Angiography was helpful in 21% of cases by revealing lesions undiagnosed clinically; in 9% by failing to confirm a clinical diagnosis which might otherwise have led to exploration of the neck; and in 20% by giving support to the clinical diagnosis which is of value when definitive treatment is contemplated.

Against this positive help must be weighed the hazards of angiography.

Some workers (Segelov 1956, Silver 1957, Kuhn 1959) consider that neither mortality nor morbidity is associated with it. On the other hand Broadbridge and Leslie (1958), in a series of 800 angiograms in which the neurological sequelæ were carefully recorded, found a complication-rate which varied from 9 to 14% according to the radio-opaque medium employed. Dimant et al. (1956) observed 2 deaths and 16 other complications in a series of 1007 angiograms, 4 of the complications arising in patients with arteriosclerosis; and Frantzen et al. (1959) had 1 death after angiography in a series of 93 cases of cerebral apoplexy, although they avoided patients in poor condition. Moreover Segelov (1956), in reviewing nine reported series which comprised 3788 angiograms in all, found 22 deaths and 81 other complications.

The reported complication-rate depends largely on the method of assessment. If, for example, angiography is performed by a radiologist and the patient's condition worsens after his return to the ward, the radiologist may not be informed. A retrospective perusal of case-notes is likewise not an adequate means of making such an assessment. Deciding what complications should be attributed to angiography is also difficult; those who report no morbidity presumably attribute continuing deterioration of a patient after angiography entirely to the natural development of his lesion, and apportion none of it to the angiogram.

We looked specially for increase in the clinical deficit of our patients during the twenty-four hours following angiography, and any such increase was attributed to the procedure. This method of assessment loads the scales against angiography but has the merit of being objective and of not belittling the risks. We found a complication-rate of 11%, all the complications being transient.

At present it is impossible to strike an exact balance between gain and loss when using angiography in the management of acute strokes. Much depends upon the treatment contemplated. If this is to be confined to general supportive measures, angiography is of limited

value, serving only to reveal occasionally an aneurysm, arteriovenous malformation, subdural hæmatoma, or tumour which may present as a stroke. If, on the other hand, more specific lines of treatment are envisaged, greater diagnostic accuracy than can be attained clinically is necessary. The problem is to assess the value of these specific lines of treatment. Initial enthusiasm for anticoagulant therapy has been somewhat tempered by later studies (Carter 1959). Similarly McKissock et al. (1959) have shown that the surgical treatment of cerebral hæmorrhage carries an immediate mortality of about 50% and an overall mortality of about 75%; but, as they point out, no adequate figures for the results of conservative treatment are available for comparison. Hence, until the value of the various forms of treatment is known, the place of angiography as a step towards definitive treatment cannot be finally assessed.

Meanwhile angiography is clearly not justified for all patients with an acute stroke, but centres with the facilities should continue their endeavours to assess the place of angiography in the management of acute strokes in relation to the methods of treatment available.

Summary

A consecutive series of 80 patients was submitted to angiography within seventy-two hours of the onset of an acute stroke. In 33 cases the angiogram provided evidence of a specific lesion, and 17 of these had not been diagnosed by the clinician. Complications arose after angiography in 9 patients.

Now that specific methods of treating patients with acute strokes are available, angiography is important as an aid to accurate diagnosis. The place of angiography cannot be finally assessed until the value of the various forms of treatment is known.

We wish to thank Sir Charles Symonds for helpful criticism, and the trustees of the Nuffield Foundation for their generous support of our studies of cerebrovascular disease, of which this forms a part.

Some of the results of this investigation were communicated at a Conference at the Royal College of Physicians, the proceedings of which are to be published by the Pitman Medical Publishing Co. Ltd.

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". . . I believe that the establishment of departments of general practice is a retrogressive measure . . . Its major defense, that it requires a generalist to teach students the ways of general practice, is delusionary. Medical schools should train their undergraduate students in sound basic principles of medicine, with enough experience with sick persons to enable the graduate to get on with his training for practice, for research, or for teaching, or for all three. To try to turn out a physician ready for any of these careers upon graduation is to oversimplify a complex problem."—WILLIAM B. BEAN, *Northwest Medicine*, 1959, **58**, 538.

UPPER END OF RANGE OF INTELLIGENCE IN MONGOLISM

M. I. DUNSDON
M.A. Reading, Ph.D. Lond.

C. O. CARTER
B.M. Oxon., M.R.C.P.

R. M. C. HUNTLEY
B.A. Brist., B.Ed. Edin.

From the Clinical Genetics Research Unit, Medical Research Council, Institute of Child Health, The Hospital for Sick Children, Great Ormond Street, London, W.C.1

OPINIONS differ concerning the upper end of the range of intelligence in mongols. Some would maintain that none are above imbecile level; others that a significant proportion are only feeble-minded. The only intelligence distribution known to us, taken from a large unselected series, is that of Øster (1953).

He gives intelligence quotients for 35 of his series of over 600 mongol children. These 35 children were not specially tested for his survey, but intelligence-test results were found in their medical records. It is not known why they were selected for testing. Reading from the diagram published, it appears that 5 of these had test scores of 50 or over, the highest (63) being obtained by a child of 8.

Wallin (1949), in surveys of mentally retarded children between 1921 and 1929, found 23 mongol children attending schools in Ohio and 26 mongol children attending schools in St. Louis. The highest I.Q. in this group was also 63, the range being from 19 to 63.

1 child has been reported as being a mongol with an intelligence-test score well over 100 (Cant et al. 1953). But later examination of the palm prints of this child gave no support to the diagnosis of mongolism.

A follow-up of all the mongol children attending The Hospital for Sick Children between 1945 and 1950 provided an opportunity to select those who were apparently brightest, and to test their levels of intelligence. The opportunity was also taken to relate these children's achievements in formal education to their intelligence scores and ratings on a social maturity scale.

It is of interest to know whether mongol children who are relatively high-grade intellectually differ physically from other mongols. Most of the stigmata of mongolism are not easily measurable, and so their assessment is largely subjective. An exception is the measurement of the position of the "t" triradius on the palm prints (ATD angle, Penrose 1954). Measurements of this angle made on mongols found to be relatively high-grade have been compared, therefore, with those made on matched controls from the remainder of the series and with those from a large series reported by Penrose.

The Sample

The mongol children from whom the selection was made included 224 who attended the hospital between 1945 and 1950 and who were alive in 1954. An account of the types of care and disposal provided for children in this group by July, 1954, has been given previously (Evans and Carter 1954). In 1956, when this group was reviewed, 214 were still alive and at least 5 years old, as were also 176 of an additional series of 306 who had attended the hospital between 1951 and 1955, affording a total sample of 390 available for further investigation.

The provision made for these children in 1956 is shown in table I. Of this number, 52 were selected for testing: they included 8 of the 9 then in primary schools (the 9th being known not to be high-grade), all the 23 in schools for the educationally subnormal (hereinafter called E.S.N. schools), and 2 awaiting places at such schools. It was thought that these would include nearly all who might be high-grade, since all who had been assessed as educable would be included. In addition, 12 of the 15 attending private schools were selected, in case some of these also might be high-grade: of the 3 others, 2 were known not to

TABLE I—EDUCATIONAL OR OTHER PROVISION FOR 390 MONGOL CHILDREN AT THE TIME OF SELECTION IN 1956

Age (yr.)	Primary school	*E.S.N. school	Occupation centre	Home tuition	Institution	Fostered low-grade	Awaiting admission			Not yet assessed	Private school	Private institution	Parents refused offer of place in		Total
							*E.S.N. school	Occupation centre	Institution				Occupation centre	Institutions	
5	2	1	26	..	7	2	..	12	1	7	5	1	2	..	66
6	4	1	30	1	6	1	1	10	1	1	..	..	2	1	59
7	..	2	29	1	7	..	..	3	..	2	2	..	3	1	50
8	1	6	32	..	9	..	..	1	2	..	2	..	5	..	58
9	1	3	26	..	11	..	1	..	..	..	2	..	2	..	46
10	1	5	28	1	9	..	..	2	..	..	2	..	2	..	50
11+	..	5	35	4	11	..	..	1	..	1	2	..	2	..	61
Total	9	23	206	7	60	3	2	29	4	11	15	1	18	2	390

* School for the educationally subnormal.

be high-grade and 1 could not easily be brought to the hospital. Another 7, either at an occupation centre, or being taught by a home-teacher, or awaiting assessment, were included as possibly high-grade. The parents of 8 of the 52 selected children did not accept an invitation to bring their children for testing: 3 of these children were at private schools, 3 at primary schools, and 2 at E.S.N. schools, leaving a total of 44 who came for assessment. These 44 children were tested between June, 1957, and March, 1958, within two years after selection.

Procedure

The children and one or both parents were interviewed. During the interviews the children were given the following standardised tests: for intelligence, form L of the Terman-Merrill (1937) revision of the Stanford Binet scale; for social maturity, the Vineland social maturity scale, Doll (1936); for basic educational achievement, Burt's reading-accuracy and oral-arithmetic tests. The parents were asked about their children's responses to demands made on them at school or occupation centre, and at home, and how adaptable they were to less familiar situations.

Results

INTELLIGENCE

The distribution of I.Q.s and chronological ages at date of test are shown in table II. The majority of the children were aged between 8 years 6 months and 14 years 5 months. 3 patients (all boys) were aged 16 years or more; of these, 1 (aged 16 years) was still at a private E.S.N.-type boarding-school, and the others (aged 17 years 1 month, and 17 years 7 months) had only recently left E.S.N. schools.

The I.Q. range was from under 25 (lowest score 19) to over 65 (highest score 68). All but 9 of the 44 patients who could be tested had I.Q.s between 35 and 54: 20 had I.Q.s of 45 or over, including 5 with I.Q.s of 55 or over (1 of these [chronological age 17 years 7 months] having an I.Q. of 68). The I.Q. ranges for boys and girls were essentially similar.

To these results may be added I.Q. estimates kindly supplied by medical officers of health for 6 of the 8 children who did not attend for interview and for 2 children who, since selection, had been transferred from an occupation centre to an E.S.N. school. Of the 3 at primary schools, 1 had an I.Q. of 65; the I.Q.s of the other 2 were not known; the 2 already at E.S.N. schools had I.Q.s of 48 and 46; of the 3 at private schools 1 had an I.Q. of 48, and 2 were too low-grade to be assessed; the 2 who had been transferred from occupation centres to E.S.N. schools had I.Q.s of 54 and 53.

If we are correct in assuming that few of the more intelligent mongols in the total sample of 390 were missed, these figures indicate that 26 in 390—that is between 6 and 7%—had I.Q.s of 45 and over, though only 1–2% had I.Q.s above 54. If an I.Q. of 45 is taken as the minimum level at which a child has a reasonable chance of deriving benefit from education in an E.S.N. school, then it would seem from this series that 6–7% of mongols should at least be considered for this type of school. Some, however, will be unsuitable on grounds other than intelligence.

TABLE III—I.Q. AND EDUCATIONAL PROVISION AT TIME OF INTELLIGENCE TEST IN 1957–58

I.Q.	*E.S.N. school	Private school	Occupation centre	Home	Total
65–69	1	..	..	..	1
60–64	..	..	..	..	..
55–59	4	..	..	..	4
50–54	5	1	..	†1	7
45–49	4	2	2	..	8
40–44	3	2	5	2	12
35–39	2	1	4	..	7
30–34	..	2	..	..	2
25–29	1	..	..	..	1
Under 25	..	..	..	1	1
Untestable	..	1	..	..	1
Total	20	9	11	4	44

* School for the educationally subnormal.
† No school for the educationally subnormal locally available.

SOCIAL MATURITY

The Vineland social maturity scale, which tests assets other than the purely intellectual, was chosen as a useful measure of the effectiveness with which the child man-

TABLE II—CHRONOLOGICAL AGE AND INTELLIGENCE QUOTIENT OF 44 SELECTED MONGOLS * AT TIME OF TESTING IN 1957–58

C.A.	I.Q.s											Total
	Under 25	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	Untested	
5[6]–6[5]	..	..	..	..	1	..	..	..	..	..	..	1
6[6]–7[5]	..	..	..	..	1	..	..	2	..	..	..	3
7[6]–8[5]	..	..	..	..	..	..	1	..	..	..	..	1
8[6]–9[5]	..	..	..	..	..	3	1	..	..	..	1	5
9[6]–10[5]	..	..	1	2	2	1	1	1	..	..	..	8
10[6]–11[5]	..	..	..	2	4	1	3	..	..	..	..	10
11[6]–12[5]	1	..	..	1	1	2	..	..	..	..	..	5
12[6]–13[5]	..	..	..	1	1	..	1	1	..	..	..	4
13[6]–14[5]	..	..	..	1	2	1	..	..	..	..	..	4
16[6]–17[5]	..	1	1	..	..	..	..	..	..	..	..	2
17[6]–18[5]	..	..	..	..	..	..	..	..	..	1	..	1
Total	1	1	2	7	12	8	7	4	..	1	1	44

C.A. = chronological age in years and (superior numerals) months.
* Information is given in the text on the further 8 children who were selected, but did not attend for interview.

aged his environment. Doll (1935) defines the purpose of his scale as being to measure the extent to which a person progressively dominates his environment and creates, demands, or justifies his own freedom of action as age increases. The scale is not designed to measure the results of specific training as such, and scores are not necessarily improved by the affording of opportunities which the child cannot of his own volition use to advantage.

The scores of the mongol children on the test are shown in table IV, expressed as social age (S.A.) and social quotient (S.Q.), (the mean social quotient for a random sample of children lies around 100).

EDUCATION

Provision at Time of Interview

The children came for test and interview up to two years after their selection as possibly high-grade, during which time there had been several changes in the types of provision made for them. A distribution of placement at the time of the test, in relation to I.Q., is shown in table III. All the 6 children originally attending primary schools had been transferred—3 to E.S.N. schools, 1 to a private school, 1 to an occupation centre; and 1, a low-grade defective, was at home. Most of the children in E.S.N. schools and private schools of E.S.N. type had kept their places. This was true of all 8 who, on test, were found to have I.Q.s of 50 or more; while, of the 4 with I.Q.s of 45–49, 1 had moved to an occupation centre.

In this series, only 2 children with I.Q.s between 45 and 49 were at occupation centres; but this was due, in some degree, to the fact that, unless there was reason to suppose that they were high-grade, children at occupation centres were not chosen for test and interview.

Response to Education

The educational attainments of the 20 children in the E.S.N. schools, measured by " reading age " and " arithmetic age ", are shown in columns 6 and 7 of table IV, in relation to sex, chronological age, mental age, and social-maturity age. Arithmetic scores were consistently low. Only 1 child (the boy with an I.Q. of 68) achieved an average 6-year-old level, and only 7 could manage addition of units with the accuracy of an average 5-year-old. Achievement in reading was more varied. 5 children obtained word-recognition accuracy scores which ranked only a year or two behind those normal for for their ages, and it is noteworthy that all these children had both intelligence and social maturity quotients of 50 or more.

TABLE IV—MENTAL AGE, SOCIAL AGE, INTELLIGENCE AND SOCIAL QUOTIENTS, AND EDUCATIONAL ACHIEVEMENT OF 20 MONGOL CHILDREN ATTENDING E.S.N. SCHOOLS

I.Q. group	Sex	C.A. (yr. and mth.)	M.A. (yr. and mth.)	S.A. (yr. and mth.)	I.Q.	S.Q.	R.A. (yr.)	A.A. (yr.)	E.R.
45 or over	M	17 7	10 2	11 3	68	64	10 1/2	6	S
	F	14 3	6 2	7 2	45	51	8 1/2	5	S
	M	12 6	6 11	7 2	55	58	11 1/2	5	S
	F	12 2	6 2	8 4	51	69	8	5	S
	M	11 10	5 9	7 4	49	62	7	5	S
	M	10 9	5 9	6 6	53	60	9	5	S
	F	10 8	5 8	8 0	53	80	7 1/2	5	S
	M	10 0	5 8	7 5	57	75	9	5 1/2	S
	M	11 1	5 7	4 4	50	39	..	..	U
	F	10 0	5 3	..	53	..	..	..	U
	F	8 9	4 2	6 3	48	60	..	..	U
	F	8 7	4 1	4 6	48	52	..	..	U
	F	6 11	4 0	2 9	58	42	..	..	U
	M	6 10	4 0	2 4	59	35	..	..	U
Less than 45	F	13 7	5 8	7 2	42	53	..	..	U
	M	12 3	5 0	5 4	41	44	..	..	U
	M	11 1	4 9	6 0	43	54	6	..	S
	F	11 11	4 3	7 4	36	62	..	..	U
	M	17 1	4 2	4 8	28	32	..	..	U
	F	9 10	3 7	6 0	36	61	..	..	U

C.A. = chronological age. A.A. = arithmetic age.
M.A. = mental age. E.R. = educational response.
S.A. = social age. S = satisfactory.
R.A. = reading age. U = unsatisfactory.

TABLE V—ATD ANGLES IN " BRIGHT " MONGOLS (I.Q. 45 OR MORE), " NOT BRIGHT " MONGOLS, AND A CONTROL MONGOL SERIES

Sum of ATD angles (degrees)	Bright		Not-bright		Penrose's series	
	Boys	Girls	Boys	Girls	Boys	Girls
200	..	..	..	2	..	..
195	..	..	..	..	1	1
190	..	..	2	1	..	1
185	..	..	..	1	..	..
180	..	1	..	1	4	2
175	2	..	3	2	3	4
170	..	2	2	2	3	2
165	1	1	1	..	5	3
160	..	2	3	1	8	6
155	..	1	1	2	9	8
150	2	1	..	2	7	4
145	1	..	5	..	3	1
140	1	..	3	..	6	4
135	..	..	2	2	4	3
130	..	..	2	2	3	1
125	1	..	1	2	3	2
120	..	..	..	1	1	1
115	2	1	1	1	2	1
110	..	..	1	1	2	..
105	..	..	1	..	..	..
100	..	..	..	..	1	2
95	..	..	..	2	2	4
90	..	..	..	2	2	1
85	..	..	1	1	3	..
80	..	1	1	2	2	1
75	..	..	..	..	1	1
70	..	..	..	..	..	2
Total	10	10	30	30	75	55
Mean	147·5	152·5	146·7	140·5	143·5	143·3
S.D.	22·3	30·3	27·3	37·3	28·6	31·9

In column 7 of table IV is shown an estimate of the satisfactoriness or unsatisfactoriness of the children's response to education, based on their educational achievements and information given by their parents. Of the 6 children with I.Q.s less than 45, only 1 was making a satisfactory response; of the others, 2 or 3 may well have been allowed to remain in E.S.N. schools because of their relatively good social development. Of the 14 with I.Q.s of 45 or more, 8 were making a satisfactory response and 6 an unsatisfactory response. Table IV shows that, in this group with I.Q.s of 45 or over, response to education was more closely related to social quotient than to intelligence quotient alone. The mean I.Q. for the satisfactory group was 53·9 and for the unsatisfactory 52·7; the mean social quotients were 64·9 and 45·6 respectively. The series is small, but the results suggest that a mongol child may need a social quotient of 50 or more, in addition to an I.Q. of at least 45, in order to profit much from attendance at an E.S.N. school.

PHYSICAL STIGMATA IN HIGH-GRADE MONGOLS

Some have thought that mentally high-grade mongols have fewer of the stigmata of mongolism than have mentally low-grade mongols; others that high-grade mongols have even more pronounced stigmata of mongolism than mongols in general (see Gibson and Gibbins 1958). There is obviously a danger of bias in that those diagnosing mongolism may require more stigmata in a relatively bright child than in an obviously retarded one.

It is possible to test these hypotheses objectively for one sign of mongolism—the ATD angle on the palm prints (Penrose 1954). This (apart from a chromosome count) is the most reliable single sign of mongolism, but was not used by the physicians making the diagnosis in this series.

The distribution of this angle measurement, summed for the two hands for the " bright mongols " (10 boys and 10 girls) in this series who achieved I.Q.s of 45 or more is shown in table V. This is compared with the distribution for 60 mongols, matched for sex and age, taken at random

from the remainder of the series, and also with the distribution for patients of about the same age-range (5–14 years) in Penrose's (1954) series. It will be seen that the relatively bright mongols have a distribution of ATD angles essentially similar to both control series.

Conclusion

The upper limit of the intelligence range of mongolism appears to be a Terman-Merrill quotient of approximately 70. If a patient with a substantially higher intelligence is thought to be a mongol, this should be tested by a chromosome count. On the analogy of Klinefelter's syndrome (Ford et al. 1959) there may possibly be partial mongols with some cells having a chromosome count of 47 and others of 46, or there may be forms of mongolism in which only part of the chromosome is reduplicated.

We have the impression that there is little correlation between degree of physical stigmata and intelligence level in mongolism, though we have been able to demonstrate this objectively only for the ATD angle on the palm prints.

It is of some administrative importance that there is a small but significant proportion of mongol children (6 to 7% in the present sample of nearly 400) with intelligence quotients within the range usually considered suitable for schools for the educationally subnormal. Since leaving an E.S.N. school, the patient with the highest score in this series has lived with his mother and, for three years, has held a job in a saw-mill. Some of the "intellectually brighter" mongols are, however, too unstable or immature in social development to profit from this form of education. In this series a close association was found between educational failure and social quotients of less than 50, even when the intelligence scores were at least 45; it would therefore seem worthwhile to examine more closely the predictive value of the social maturity scale in selecting mongols for E.S.N. schools.

Summary

In order to estimate the upper limit of the range of intelligence found with mongolism, 52 mongol children from a group of 390 were selected for testing; and, of these, 44 came for interview and test. The selected children were all those who had attended primary schools, private schools, and schools for the educationally subnormal, and a few others who had seemed relatively bright at interview.

The highest I.Q. found on the Terman-Merrill test was 68 for a youth aged 17 years 7 months. The proportion of those with I.Q. scores of 45 and over in the original sample of 390 was estimated to be 6–7%, and of those with I.Q.s of 55 and over, 1–2%. The upper limit of the range of Terman-Merrill intelligence quotients found among mongol patients is probably in the region of 70.

Tests of educational achievement and interviews with the parents showed that 8 of the 14 with intelligence quotients of 45 and over who were at schools for the educationally subnormal were making a reasonably satisfactory response to that type of education. In this group the response to education was more closely related to social quotient (measured by the Vineland scale) than to intelligence quotient alone.

Mongol children, to have a reasonable chance of profiting satisfactorily from the education provided for the educationally subnormal, need, besides an intelligence quotient of not less than 45, a social quotient of the order of at least 50.

The ATD angles on the palm prints of the 20 patients with intelligence quotients of 45 or more were essentially no different from those found among patients with lower intelligence-test scores. No association was found between the degree of this stigma of mongolism and the degree of mental retardation.

We wish to thank members of the staff of The Hospital for Sick Children for access to their patients; Mrs. K. A. Evans, whose study of the educational provision for these patients made this study possible; and Dr. J. A. Fraser Roberts and Professor Alan Moncrieff for their interest and encouragement. We are much indebted to the medical officers of health of London and the home counties for their help in tracing patients. We also wish to thank the National Birthday Trust Fund and the Sir Halley Stewart Trust for grants towards the cost of the survey on which this study is based.

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SIGNIFICANCE OF REDUCIBLE INGUINAL HERNIA IN CLOSED ABDOMINAL INJURIES

H. T. JOHN *
D.F.C., M.B. Durh., F.R.C.S.
SENIOR SURGICAL REGISTRAR, BRISTOL ROYAL INFIRMARY

DESPITE the excellent review by Aird (1956), and several other articles, the significance of a reducible inguinal hernia in closed injuries of the abdomen is often not appreciated. I should like to re-emphasise the significance of such a hernia in assessing what may appear to be comparatively minor abdominal trauma.

Rupture of the small intestine may complicate a pre-existing easily reducible inguinal hernia following a sudden strain or direct trauma to the abdominal wall. In the first case reported below a loop of small bowel was damaged after a minor blow to the abdomen; in the second the bowel was found to be perforated after a sudden violent contraction of the abdominal wall.

Case-reports

Case 1.—In 1954 a healthy middle-aged man was struck a glancing blow in the back by a hurrying man while waiting on a railway platform. He felt shaken afterwards and had some mild generalised abdominal pain. When seen in the casualty department of University College Hospital he was tender over the lower abdomen, but there was no rebound tenderness, and the gut sounds were normal. A left inguinal hernia was noted which he said he had had for very many years and which had never caused trouble. The hernia was easily reducible and not tender.

He was admitted to hospital, and during the next few hours his temperature rose to 99° and his pulse-rate to 110 per min. Tenderness spread over the lower abdomen, he developed guarding and rebound tenderness, and his gut sounds became much fainter.

At laparotomy, 12 hours later, a loop of ileum lying free in the abdominal cavity near the orifice of the inguinal hernia was found to have perforated on its anti-mesenteric border. For about 3 in. on either side the bowel was reddened and swollen, with multiple ecchymoses over both the bowel and a triangular area of mesentery based on the loop (see figure). The perforation was closed, and the patient made an uneventful recovery.

Case 2.—A fit man, aged 51, attended the casualty department of the Royal Devon and Exeter Hospital in 1958, having slipped while descending a ladder and fallen astride a plank. He did not sustain direct injury to his abdomen, but he had

* Present address: Peter Bent Brigham Hospital, 721, Huntington Avenue, Boston, 15, Massachusetts, U.S.A.

made violent efforts to save himself. He walked into hospital for a check-up, complaining only of slight abdominal pain. Apart from mild generalised lower abdominal tenderness and an easily reducible right inguinal hernia, nothing abnormal was found. He fainted shortly afterwards and was admitted to hospital for observation.

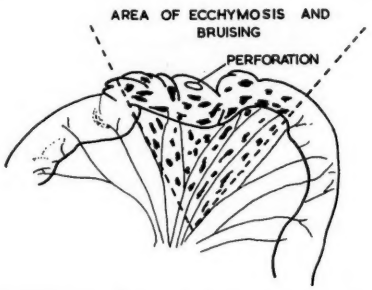

Diagram to show changes in the ileal loop in case 1.

In the ward he was carefully examined again, and found to have guarding and mild rebound tenderness. At laparotomy the findings were similar to those of case 1. A loop of ileum about 2 ft. from the ileocæcal valve, and lying free near the orifice of the hernia, had perforated on its anti-mesenteric border. Ecchymoses extended over about 6 in. of bowel around the perforation, and a triangular area of mesentery was contused. The distance from the bowel to the apex of this triangle was about 4 in. The perforation was closed, and the patient made an uninterrupted recovery. His hernia was repaired later.

Discussion

In the past century many ruptures of the bowel after attempts to reduce incarcerated herniæ were reported (Aird 1956). Such reports have now become rare, but about thirty-five cases have been described of perforation of the bowel associated with inguinal hernia after closed injuries of the abdomen from trauma applied a distance from the hernial sac, or after a sudden violent muscular strain.

All these patients were healthy well-built men, and no such cases have been described in women. The herniæ were all inguinal and nearly always right-sided. Apart from one case reported by Scarpa in 1823 and cited by Aird (1956) in which the colon was injured within the sac, all the perforations have involved small bowel. In most cases the damaged loop was found within the abdominal cavity near the orifice of the inguinal sac. The lower ileum was injured most often, but any part of the small bowel may be involved. The perforation usually took the form of a tear of the anti-mesenteric surface, though in two cases the injury was at the site of the mesenteric attachment. According to Aird (1935, 1956) the mucosa surrounding the perforation pouts outwards, being gripped by the muscular coats, and the bowel on either side of the perforation may be bruised.

Several explanations of the mechanism of rupture are possible in such patients.

Older theories (Kahn 1914, Lockwood 1923) suggest that a fixed loop of bowel is more susceptible to injury than a mobile one. At the time of injury the bowel is actually within the inguinal sac, fixed at one end by its attachment within the abdomen and at the other by contraction of the muscles surrounding the neck of the sac. Thus the fixed length of bowel would sustain injury and not the loop within the hernial sac. After the injury the muscles relax and the bowel slips back into the abdominal cavity.

Bange in 1937 (cited by Aird 1956) suggested another theory to explain those cases in which the bowel lies free in the abdominal cavity and is thought not to have been in the sac at the time of injury. He pointed out that a sharp rise in intra-abdominal pressure causes an equal increase in pressure within and without the bowel wall in the normal abdomen, thus preventing rupture of the bowel. But in the presence of an inguinal hernia the wall of any bowel lying close to the orifice is unsupported. Thus rapid increase of intra-abdominal pressure will cause rupture at this point. Bange described an experiment in which he placed a partly inflated balloon within the barrel of a syringe, and showed that, when the nozzle was occluded by a finger, increase of pressure within the barrel caused no damage to the balloon. But once the finger was removed the balloon perforated near to the orifice of the nozzle.

As neither of these explanations fully accounts for the widespread changes in both the loop of bowel and its mesentery, I repeated Bange's experiment using bowel instead of a balloon.

The intact small bowel of a cat, which had been killed after experimental studies, was removed and tied off at both ends, and then about 30 ml. of air was injected into its lumen. It was placed in the barrel of a large syringe, the plunger was inserted, and a fingerstall was tied over the nozzle. Despite many attempts to perforate the bowel by a great and rapid increase of pressure within the syringe barrel, it was not possible to damage it. The experiment was repeated using an isolated loop of cat's small bowel 4 in. long. This was placed within the syringe and a high pressure was produced within the barrel. This time the bowel wall split at the apex of the loop opposite the orifice of the nozzle.

The experiment involving the whole length of small bowel seems to correspond more closely to conditions within the abdomen than did Bange's experiment, and Bange's explanation is probably not correct. The widespread changes in the bowel wall and the damage to the mesentery seem to delineate an area which would be appropriate if that loop were actually within the sac at the time of injury.

Bruce (1942) reported a case in which the damaged bowel seemed to have first discharged within the hernial sac, lending support to the view that the loop is within the sac at the time of injury. With a sudden great increase of intra-abdominal pressure the intra-luminal pressure will increase within the whole of the bowel. The pressure in the lumen of the loop within the sac will be opposed only by the atmospheric pressure outside the sac, and may well perforate. The same mechanism, aided by mesenteric constriction from contraction of the muscles around the neck of the sac, leads to the ecchymoses so commonly found. This explanation accords well with the findings of perforation at the apex of the loop and vascular changes in the mesentery and bowel loop. As the muscles relax the bowel slips back into the abdominal cavity, and this may be aided by increase of pressure within the sac due to the perforation.

Shortly after injury the symptoms and signs of intraperitoneal damage are often slight or absent, and at this stage it is all too easy to dismiss any slight pain or tenderness as due to trauma to the abdominal wall itself. Gross signs may not appear for many hours, presumably because the pouting mucosa is tightly gripped by the muscle coats, preventing much contamination at first. Case 1 was observed for about 12 hours before unequivocal signs of intraperitoneal damage appeared and laparotomy was undertaken. Case 2 was nearly sent home and he was admitted for laparotomy only because of the experience gained from the first case. But these examples show that any injured patient with abdominal symptoms, however slight, and a reducible inguinal hernia should be viewed with suspicion until damage to the small bowel has been excluded.

Summary

Two cases are described in which rupture of the ileum complicated a reducible inguinal hernia after closed abdominal injury.

The most likely mechanism of injury to the bowel in these circumstances is that a sudden and great increase of intra-abdominal pressure increases the pressure within all the bowel, but because the pressure inside the hernial loop is opposed by atmospheric pressure only, this loop may well perforate.

In patients with abdominal injuries and a reducible inguinal hernia, damage to the small bowel must be carefully excluded.

I should like to thank Mr. H. R. I. Wolfe and Mr. A. C. Gairdner for permission to publish these case-reports.

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PERIPHERAL VASCULAR DISEASE TREATED BY AMNION IMPLANTATION

A REVIEW OF 100 CASES

E. TROENSEGAARD-HANSEN
F.R.C.S.
LATE RESEARCH FELLOW IN SURGERY,
CHARING CROSS HOSPITAL, LONDON, W.C.2

IN an earlier report on amnion implantation for peripheral vascular disease (Troensegaard-Hansen 1956) it was stated that 80% of the cases described improved postoperatively.

Gow (1956) reported twelve cases. Rowling (1958) described eight, and Webb-Jones (1958) a small series. All maintained there was subjective improvement. Gow performed arteriograms which showed no change, Webb-Jones said that both objective and subjective improvement had taken place; he mentioned an oscillometric increase, and regarded the subjective relief in his own series as so striking that it merited further work. Rowling pointed out that in his cases, the walking distance was greatly improved; in one case it increased from 20 to 800 yards. Furthermore, the interval that elapsed after a patient stopped and before he could walk on was diminished from 10 to 2 minutes. He also mentioned that after one patient with a 4-year history of cardiac disease was treated by amnion implantation his cardiac symptoms improved considerably.

Moore (1957) described seven cases of claudication, with discoloration of the feet, in which no improvement had taken place after amnion implantation. He discontinued the treatment. Unger-Hamilton (1957) thought the poor results in Moore's series were due to the disease being advanced. He mentioned seven other patients with claudication who improved after implantation; three of them had cardiac disease and they also improved as regards cardiac tolerance. One case of erythrocyanosis improved considerably, the reddening and aching, which had been severe before operation, becoming less. Foote (1956) reported that acrocyanosis had improved after amnion implantation. Lastly, Mansbridge (1956) and Gaster (1956) described cases where the dorsalis-pedis pulsation returned after implantation, the considerable improvement being well maintained. In one of Mansbridge's cases the walking distance had increased from 100 yards to 2 miles.

The present series of a hundred unselected cases were assessed at various intervals after operation, the longest being 7 years and the shortest 6 months. In 70% more than 12 months have elapsed since operation. Improvement has been based on changes in symptoms and signs, tolerance to exercise, and special tests such as isotope-clearance and oscillometry. The results were also assessed by an independent observer. Objective improvement was noted in fifty, subjective improvement only in thirty-two, and no improvement at all in eighteen.

Clinical Material

Ninety-two men and eight women with varying degrees of intermittent claudication were treated by implantation of human amnion. They were divided into two groups. Those moderately affected comprised group II, and those severely affected comprised group III (Boyd's [1949] classification amended—see later). Thirty-seven were in group II, and sixty-three in group III. Six patients have since died from other causes.

Ninety-eight patients had arteriosclerosis and were aged 40–75 years. Two patients with Buerger's disease were under 40. No patient with a sudden onset of symptoms was included in this series, as it is well known that such cases often improve spontaneously. Fifteen patients of this series, who had previously been subjected to lumbar sympathectomy with a resulting warm foot but without amelioration of their claudication, were implanted with amnion. The results have been compared with a similar control group not treated by amnion implantation. Ten other patients, used as additional controls, were implanted with human peritoneum.

An ideal type of patient for amnion implantation is one between 50 and 60 years old, and 6 months' to 2 years' history and a walking distance of 50–200 yards (he *can* walk farther but in pain).

History

One of the features to be noted in the history of claudication is that the feet generally become cold after prolonged walking. Most patients in this series had calf pain, in the medial head of gastrocnemius, some had buttock pain, and a few had pain in the front of the leg.

It is important to be clear about the meaning of *rest pain*. It is a diffuse, persistent, and intense pain, a sign of severe ischæmia and impending gangrene, usually confined to the toes but sometimes involves the forefoot. It is not to be confused with nocturnal cramp, which disappears with exercise.

Clinical Examination

In addition to routine examination, the colour of the legs and feet, and any ulceration, should be noted. Angina, other cardiac disturbance, or anæmia should be sought for.

The peripheral pulses are palpated and the level at which the pulses disappear is recorded. The pulses should be palpated before and after operation under strictly identical conditions (e.g., of rest and room temperature), otherwise the findings are valueless.

Temperature changes can be measured with a skin thermometer, even down to 1°C.

Auscultation over the aorta or femoral artery may reveal a bruit which denotes narrowing of the vessel concerned. If no bruit is heard in the presence of arterial narrowing, it can sometimes be made to appear after forced exercise.

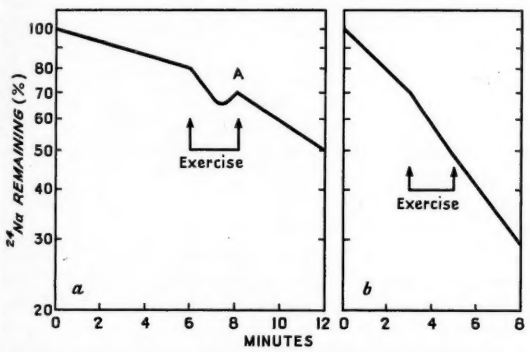
Leg-raising test.—Proximal to a block the head of pressure is high whereas distally it is low, so that on raising the limb the distal low pressure cannot overcome gravity and the limb appears pale. In this test, in which the limb is raised to 90° from the horizontal, the interval in seconds which elapses before the limb becomes pale is termed the paling interval. The foot of a patient with arterial obstruction may become pale after as little as 10 seconds, or up to 45 seconds may

elapse before paling appears, whereas a normal leg can be raised longer than 90 seconds before showing any appreciable pallor. Therefore a lengthened paling interval suggests an improved arterial circulation.

Oscillometry.—Digital examination will reveal the presence or absence of a pulse, but will not show whether the pulse was normal or subnormal in quality. With an oscillometer ('Pachon') one can record the number of deflections present and compare them with a similar record after operation. Oscillometry is an easy and fairly accurate means of determining the level of block, and whether it is complete or incomplete.

Tolerance to exercise.—By tolerance is meant the distance a patient can walk at a known speed without pain. For practical purposes the patient is asked to determine the number of paces (to ensure that the type of walking has not changed), the distance covered, and the time taken to evoke claudication.

Radiosodium (^{24}Na) test.—Since amnion implantation was first used at Charing Cross Hospital, some hundred and twenty isotope tests have been done to measure the clearance in normals and in claudicants. Typical curves before and after implantation are seen in the accompanying figure. In this



Radiosodium tests in a patient with intermittent claudication of the right leg (*a*) before treatment and (*b*) after amnion implantation.

series forty-two patients have had sodium tests, and twenty-three of these have had both preoperative and postoperative tests (Troensegaard-Hansen 1956).

In some cases radiography, electrocardiography, and temperature recordings of the legs and feet are also desirable. Hæmoglobin levels were estimated wherever anæmia was known or suspected.

Grouping of Cases

Group I is rarely seen in hospitals. Clinically it comprises patients who can "walk off" their pain, and usually there are no other symptoms or signs. These patients do not need amnion implantation as a rule.

Group II comprises those patients who do not necessarily have to stop, but can carry on walking although in pain. No colour changes are seen. Paling does not usually appear; if it does, the paling interval is long, being 45 seconds or more. Oscillations are reduced, and pain does not arise at rest. But in borderline cases the findings vary. Foot pulsation is diminished; either the anterior-tibial or posterior-tibial pulse, or both, are reduced or absent. In this series, the walking distance was 50–200 yards, the length of history from 6 months to 2 years, and the age-incidence 50–60 years. There is generalised narrowing of the arterial lumen and if there is a block it is usually incomplete, which may explain why the pulse so often returns after implantation in this group.

Group III comprises the patients who, after stopping because of calf pain, could not be encouraged to walk on. The paling interval was 15–45 seconds. There is complete arterial blockage with no oscillometric deflections. These signs will, of course, vary with the site of the block; thus a common-iliac block will register none or few oscillometric deflections over the femoral artery, and, likewise, a popliteal block will show no deflections below this level. Colour changes are present in most cases; they vary but the affected foot is usually white, or sometimes red. Warm weather makes little difference. On hanging the legs down rubor may appear. These colour changes may merge into those of the pregangrenous foot. The toes or lateral border of the foot may tingle or become numb. In this series the walking distance was 10–50 yards, the history from 2 to 5 years, and the age incidence 50–70 years.

The Operation

A 4-in. incision is made in the outer border of the upper third of the thigh of the affected leg. The amnion is inserted evenly and without much pressure into six pockets deep to the fat. The patient is kept in bed for 4 days, and normally goes home on the 6th day.

Late Management

The patient is at first encouraged to increase his walking distance but not his speed. Smoking is not forbidden but it may be reduced. Alcohol is allowed. He should not expose his feet to an open fire or use a hot water bottle. Hot baths are also discouraged.

Results

Questionnaires were completed by each of the general practitioners who referred patients for treatment by amnion implantation. Thus the final opinion of an independent assessor was obtained, stating what improvement, if any, had taken place after operation. The general practitioner is perhaps the person best qualified to judge the results of any treatment given to his patients.

Group II

Of the thirty-seven patients, thirty-four (91%) showed one or more signs of objective improvement (see table): twenty-six (70%) had oscillometric increase, fourteen (37%) had a return of foot pulsation, and eight (21%), who had a cold foot before, had a warm foot after operation. Toe-nails grew quicker with more frequent cutting, and hairs appeared over the dorsum of the phalanx in a number of cases, probably due to increased collateral blood-supply. The patient's gait became "springy", and any calf pain was transient and never severe. Walking up inclines, which was impossible before operation, was accomplished with comparative ease afterwards. All thirty-seven patients thought that their walking distance and speed had increased.

OBJECTIVE IMPROVEMENT IN PATIENTS WITH INTERMITTENT CLAUDICATION

Improvement	Group II No.	Group III No.	Groups II and III combined	Amnion implant after sympathectomy (15 cases)	Peritoneal implant (10 cases)
Returned foot pulsation	14 (37%)	2 (3%)	16%	1 (7%)	0
Improved ^{24}Na clearance	12 (32%)	4 (6%)	16%	3 (20%)	0
Oscillometric increase	26 (70%)	13 (20%)	39%	3 (20%)	0
Warm foot (previously cold)	8 (21%)	14 (22%)	22%	2 (13%)	0
Increased paling interval	..	10 (15%)	10%	0	0

SUBJECTIVE IMPROVEMENT

Increased walking distance	3 (8%)	26 (41%)	29%	7 (11%)	4 (10%)
Postoperative warm foot (previously cold)	2 (5%)	18 (28%)	20%	2 (3%)	0
Loss of rest pain	0	7 (11%)	7%	0	0
Loss of night pain, and pain not specifically vascular	12 (32%)	8 (12%)	20%	2 (3%)	0

In this group nineteen patients had sodium-clearance tests, and in twelve these were performed both before and after operation. The results showed that all twelve patients had improved, and seven of these had normal sodium-clearance after operation. The remaining seven had only one test, and four of these were normal after operation; the other three were unaltered, showing poor clearance.

Group III

Of the sixty-three patients sixteen (25%) showed objective improvement (see table); thirteen (20%) of them showed oscillometric increase, two (3%) showed improvement in foot pulsation, and fourteen (22%) had a warm foot after operation. All sixteen thought that their walking distance had increased and because of the extremely good results, they may have been borderline cases—between groups II and III. Seven (11%) patients lost their pain at rest after implantation. Patients in this group who showed objective improvement all found that walking on the flat was within their tolerance, but they could not manage uphill gradients. No morbidity or mortality has resulted from implantation.

Twenty-three group-III patients had sodium-clearance tests, eleven of whom had both preoperative and post-operative tests. Of these, four showed improved clearance and two showed normal clearance after operation; five showed poor clearance. The other twelve were patients who either showed subjective improvement only, or none on clinical grounds; they had poor clearance curves which confirmed the clinical findings.

Groups II and III Compared

A comparison between the results in group II and group III shows that whereas in group II the foot pulsation returned in fourteen patients, in group III this occurred in two patients only.

The sodium-clearance in group II improved in twelve patients, whereas this happened in four patients only in group III. Oscillometric increase was strikingly different also; in group II twenty-six patients showed improvement, whereas in group III thirteen showed comparable changes.

Re-implantation was necessary in six patients where there was subjective improvement only or none at all.

Results of Amnion Implantation after Previous Lumbar Sympathectomy

Thirty patients previously subjected to lumbar sympathectomy were divided into two equal groups of fifteen: one group had no further treatment and was used as a control, the other was implanted with human amnion. The improvement compared with the control group (in which no change was noted) was small. The control group was examined on several occasions and no change was noted and there has to date been no improvement.

Results of Peritoneal Implantation with a Control Group

Ten patients in group II were implanted with human peritoneum and the results compared with a similar control group. Two improved inasmuch as their walking distance, but not their speed, was greatly increased. This was maintained for 3 weeks, after which there was a gradual relapse. Four patients improved for 10 days only. The remaining four showed no improvement and the trial was therefore discontinued.

Discussion

Neither autoclaved amnion nor friable muconium-stained amnion, which is largely devoid of epithelium, should be used for implantation. After amnion implantation a small fall in blood-pressure of 5–15 mm. Hg has been noted. The hæmoglobin percentage rose in two cases, and severe coexisting angina improved. Assessment is here extremely difficult. The implanted leg feels warm, and a vascular hyperæmia is set up.

Prolonged exercise by any patient with claudication will be followed by muscle ischæmia and pain, and the pain will temporarily prevent exercise. If reactive hyperæmia is induced without muscle ischæmia and pain by amnion implantation, then even prolonged exercise becomes possible.

The mode of action of amnion is unknown, but the local vascular hyperæmia may be due to prolonged protein shock. The epithelium of the implanted amnion also seems to play some part, for when it is missing the results are unsatisfactory. Two possibilities arise, therefore:

1. The generalised hyperæmia may be due to sustained protein shock.

2. A specific vasodilator or muscle relaxant may be liberated when amnion tissue is absorbed into the general blood-stream.

Summary

A hundred unselected patients with intermittent claudication were treated by amnion implantation. Ninety-eight had arteriosclerosis, and two had Buerger's disease. All were in the age group 40–75, apart from the two with Buerger's disease. Eight were women.

Thirty-seven patients were moderately affected (group II) and sixty-three were severely affected (group III).

In group II thirty-four (91%) showed both objective and subjective improvement.

In group III sixteen (25%) showed both objective and subjective improvement; twenty-nine (46%) showed subjective improvement, and eighteen (28%) showed no improvement.

Of thirty patients who had been subjected to lumbar sympathectomy, fifteen were implanted with amnion and the results compared with the other fifteen who had no further treatment. Of those treated by implantation eight improved subjectively and their walking distances increased. The other seven did not.

Ten patients (all in group II) were implanted with human peritoneum. Two patients improved subjectively for 3 weeks and then gradually relapsed; four improved subjectively for 10 days only; and four derived no benefit and there were no objective findings.

Early implantation may avoid many late manifestations of peripheral vascular disease.

I should like to thank the clinical research subcommittee of Charing Cross Hospital for its support; Mr. N. Ramsay, principal physicist at the hospital, for the sodium-clearance measurements; Dr. R. Moore Patterson of the radiotherapy department for his cooperation; Dr. R. A. Hickling, Mr. N. C. Lake, Mr. D. Trevor, and Dr. J. Grier, for their helpful suggestions; Prof. A. M. Boyd for his advice and encouragement; Mr. Peter Martin for constructive criticism and help in reading and preparing this paper; and the general practitioners who referred cases and who kindly completed the questionnaires.

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LARYNGOSTOMY IN ACUTE LARYNGEAL OBSTRUCTION

PAUL ABBEY
M.B. Lond., F.R.C.S.
SENIOR REGISTRAR TO THE EAR, NOSE, AND THROAT DEPARTMENT, ST. MARY'S HOSPITAL, LONDON, W.2

RELIEF of laryngeal obstruction in its most acute form is dramatic and life saving. Although such obstruction arises infrequently, the possibility must always be borne in mind, and a clear plan of action should be ready. Many doctors have seen cases in which life would have been saved if the urgency of the obstruction had been matched by effective intervention.

Laryngostomy—i.e., an incision through the skin and cricothyroid membrane into the subglottic region—is a time-honoured procedure which has fallen into disrepute and is now performed rarely. The operation is unpopular because of the sequelæ produced by pressure if the laryngostomy tube is left in position too long; these include cicatricial stenosis, perichondritis, and inflammation of the vocal cords. But complications can be avoided if laryngostomy is used temporarily and, if a more permanent airway is required, is followed as soon as possible by tracheostomy.

The value of laryngostomy for immediate relief of sudden laryngeal obstruction in adults cannot be too highly emphasised. The procedure is simple, safe, and virtually free from complications, and it can be performed skilfully, with speed and precision, by the surgically experienced and inexperienced alike. With the skin between cricoid and thyroid cartilages first steadied between thumb and index finger, a transverse incision about $^3/_4$ in. long will expose the cricothyroid membrane. This membrane can then be incised immediately. Thus entry is gained to the subglottic region by means of two brief incisions. If no laryngostomy tube is immediately available the scalpel handle can be inserted and rotated to widen the cricothyroid space and provide an adequate airway.

The following case-reports illustrate the application of laryngostomy.

CASE 1.—A man, aged 44, was submitted in January, 1959, to direct laryngoscopy and biopsy to confirm the diagnosis of carcinoma of the larynx. Next day he had mild stridor. 36 hours later considerable laryngeal obstruction developed. An endotracheal tube relieved the obstruction, but he later pulled out this tube. When seen he was in extremis, with deep cyanosis, occasional ineffectual inspiratory efforts, and an almost non-existent pulse. Laryngostomy was carried out within seconds. After half an hour, when the patient had recovered sufficiently, formal tracheostomy was performed and the laryngostomy wound was sutured. The patient later underwent laryngectomy and block dissection, and he is now alive and well.

CASE 2.—A man of 41 attempted suicide with 'Lysol' in February, 1959, and was brought into the casualty department unconscious, cyanosed, and with laryngeal stridor. He had probably aspirated bloodstained vomit. Attempts to pass an endotracheal tube were unsuccessful, and laryngeal obstruction increased. Laryngostomy was therefore performed immediately, and bloodstained mucus was aspirated. Within an hour, when the patient's general condition had improved, and as direct laryngoscopy showed considerable laryngeal œdema, a formal tracheostomy was undertaken and the laryngostomy incision was sutured. The patient then made an uninterrupted recovery.

Discussion

Even in the most skilled hands the extremely urgent tracheostomy, with its complications, can be exceptionally difficult. A desperately ill patient whose neck cannot be extended, whose veins are engorged, in whom many tissue planes must be incised, and in whom the danger of inhalation of blood is real, presents a formidable problem. Laryngostomy avoids these difficulties. Acute laryngeal obstruction, which usually arises above the vocal cords, respects neither time nor person, and action often falls to the uninitiated. For this reason alone, laryngostomy should have a wider appeal. Moreover, the cricothyroid space, which is easy to palpate in adults, facilitates such intervention. But though laryngostomy is invaluable under such circumstances it should not supplant tracheostomy as the operation of choice for relieving laryngeal obstruction in less urgent cases.

In the cases here described laryngostomy was aimed at the temporary relief of obstruction only. After the immediate crisis, complications were avoided by elective tracheostomy performed under the more suitable conditions made possible by the initial operation. The laryngostomy wound was then sutured, healing with an almost invisible scar. A double scar in the neck is small payment for a certain and successful outcome. These cases also show that endotracheal intubation is not without dangers. In both instances the degree of laryngeal œdema was probably increased, contributing to the laryngeal obstruction.

The operation is unsuitable for children because the larynx is small and the vocal cords lie very near the site of operation, and because the cricothyroid space is difficult to define, making both immediate and delayed complications more likely.

Laryngostomy tubes are not readily available, and in hospital practice this deficiency should be rectified.

Summary

The relatively simple operation of laryngostomy is appropriate for the immediate treatment of acute laryngeal obstruction. Because it can be performed easily and quickly it should be more widely used.

Both operative and postoperative complications are avoided if laryngostomy is used only temporarily. The operation is unsuitable for children.

I wish to thank Mr. J. F. Simpson and Mr. I. G. Robin for helpful criticism, and Mr. H. S. Sharp and Dr. W. D. W. Brooks for permission to publish the case-records.

THE "SYMPHYSIS OS"

L. G. PEREIRA*
M.B. Bombay, D.Obst.R.C.O.G.
REGISTRAR IN OBSTETRICS, STOKE MANDEVILLE HOSPITAL, AYLESBURY, BUCKS

THERE are many references to the *sacral os* in obstetric literature. The examining finger finds the presenting part covered by the anterior portion of the lower segment of the uterus, while the os lies posteriorly in the hollow of the sacrum. In this condition, during labour the uterine thrust is directed towards the anterior wall, thereby producing sacculation. Labour is prolonged and many patients with this condition have finally been treated by cæsarean section.

When performing surgical induction at term, I have in the last two years observed the cervix tucked up near the symphysis pubis on three occasions. For want of a name I have recorded this finding as the *symphysis os*. It has been my practice to give 'Syntocinon' (synthetic oxytocin) by intravenous infusion to all patients the day after surgical induction, using 5 units in 1 pint of 10% dextrose if they

* Present address: Selly Oak Hospital, Birmingham, 29.

are not already established in labour. The only resistant cases to this were the ones in which the symphysis os had been demonstrated. It appears to be less common but more serious than the sacral os, which can always be made to dilate by the syntocinon drip after rupture of the forewaters.

With the symphysis os the uterine thrust in labour is directed towards the posterior wall of the lower segment, producing posterior sacculation. The patient becomes exhausted while the cervix remains undilated. A remedy for this state of things is to rupture the forewaters. Next day, if labour has not begun or been properly established, a syntocinon drip is set up in the morning. At 8 P.M., if the cervix has not begun to dilate, the drip is taken down and the patient is given enough sedation to ensure a good night's sleep.

The following morning, if labour has not begun, scalp traction is applied to the fœtus. A 1 lb. weight is used if there are pulley arrangements on the foot of the obstetric bed; but failing this, $1^1/_2$ lb. is used, with a kidney tray upside down in place of a pulley. When the cervix is firmer than usual, uneffaced and undilated so that a finger cannot be passed through the os, Hegar dilators up to size no. 6 are used before rupturing the membranes. The measures mentioned above, combined with a syntocinon drip, will induce satisfactory labour with effacement and dilatation of the cervix. When this has progressed to 3–4 fingers, the scalp traction is removed but the oxytocic drip is continued until the end of the third stage of labour.

At the time when scalp traction is applied a high vaginal swab is taken, for culture and the testing of sensitivity of any organisms found. With this precaution and the availability of antibiotic drugs, scalp traction on a full-time foetus need not be associated with the dangers described in the literature.

This method of treatment will, I am sure, save many a woman from an unnecessary cæsarean section. The technique described permits a vaginal delivery at the possible expense of a few missing follicles from the infant's scalp.

A HAZARD OF ANÆSTHESIA IN OPHTHALMIC SURGERY

F. BARNETT MALLINSON
F.F.A. R.C.S.
CONSULTANT ANÆSTHETIST, MOORFIELDS EYE HOSPITAL, E.C.1, AND PRINCESS BEATRICE HOSPITAL, LONDON, S.W.5

S. K. COOMBES
M.B. Punjab, D.A.
REGISTRAR IN ANÆSTHETICS, PRINCESS BEATRICE HOSPITAL

MOST anæsthetists who give anæsthetics for eye surgery are aware that certain pulse irregularities manifest themselves quite commonly, especially in operations on children, and more especially during strabismus operations.

These irregularities consist of bradycardia, extrasystoles, and pulsus bigeminus. They are characterised by their persistence: increase in oxygen percentage and variation in depth of anæsthesia or of agents used do not seem to have any consistent effects on them. In our experience they occur in something like 4–5% of all cases, and hitherto they have not been followed by any serious results, nor have they given rise to any anxiety.

Recently, however, we have had reason drastically to revise our attitude to what is, in effect, Aschner's reflex or the oculocardiac reflex (Aschner 1908). Evocation of this reflex is described as causing vagal stimulation, which results in bradycardia and even ventricular fibrillation (Landman and Ehrenfeld 1952). I am told that experts in the techniques of unarmed combat recognise that severe pressure on the eyes can cause syncope and, if violent enough, death.

Mechanism of Aschner's reflex.—With the exception of the extrinsic muscles of the eye, the innervation of the orbit is through the ophthalmic branch of the first division of the 5th cranial (trigeminal) nerve. The trigeminal nerve carries sympathetic and parasympathetic as well as sensory fibres (Lyle 1954). The ophthalmic nerve is also joined by fibres from the carotid plexus (Stibbe 1930). When pressure or tension is exerted on the tissues of the orbit, the afferent path of a reflex is excited—the efferent being the autonomic nerve-supply to the heart, in particular the vagus. Manipulation of the rectus muscles of the eye in mobilising and cleaning them results in tension on the orbital tissues, and this may evoke the oculocardiac reflex.

This reflex presents a hazard possibly rare but certainly clear-cut, especially in children whose vagal tone is high (Fulton 1947). The risk is also greater under anæsthesia, as in the following case:

The patient was a three-year-old child weighing 39 lb. He was a very fair, very pale boy, looking rather weak though apparently healthy and active. All systems appeared normal on clinical examination. The operation performed was " recession and resection " for convergent strabismus. Premedication was with quinalbarbitone gr. $2^1/_2$ and atropine gr. $^1/_{100}$, and the child arrived in the theatre asleep but easily roused. Induction of anæsthesia was begun by blowing nitrous oxide gently on to the face, till the patient was completely unconscious, and continued with gas-oxygen and minimal trichlorethylene through the facepiece; maintenance was with the same mixture through a pharyngeal airway. The flow of gases throughout the operation was nitrous oxide 5 litres per min. and oxygen 2 litres per min.—an oxygen percentage of 28·5. The airway was at all times clear and respiration unobstructed and adequate.

The operation took thirty-five minutes, and five minutes before it ended (during the resection of the lateral rectus muscle) the surgeon mentioned that the operative field was commendably dry. At this time the pulse showed some bradycardia (80 per min.) but nothing else abnormal. When a few minutes later the towels were removed from the patient's face we noticed that he was very pale and of a rather poor colour. The pulse was still 80 per min., and the respiration normal. Whilst the bandage was being applied the patient had a short convulsion, *not* starting in the face and involving principally the limbs. His colour became worse after this; he was therefore freely ventilated with 100% oxygen. The colour however showed no improvement, and two more convulsions occurred during the next few minutes. The patient's head was raised and 0·1 g. thiopentone given in accordance with the standard treatment for so-called " ether convulsions ". This stopped the convulsions and also the respiration, which was subsequently maintained by manual compression of the breathing bag (carried out without obstruction or difficulty through a facepiece).

There was still no improvement, and after a further ten minutes the pulse, hitherto of good volume, disappeared rather quickly. As no heart sounds were audible, the chest was opened and massage of the heart started within three minutes of its having ceased to beat. In spite of adequate circulation—evidenced by a pulse at the wrist, oozing from the wound and disappearance of the pallor—and in spite of adequate artificial respiration through an intratracheal tube, the colour remained cyanotic. During the next two hours all known measures for re-establishing normal cardiac rhythm were employed, including the defibrillator; but despite the fact that adequate circulation and oxygenation were maintained, and although the

heart was repeatedly started for periods varying from ten seconds to two minutes and even spontaneous respiration was re-established for a short time, the colour and vasomotor tone never improved. The heart seemed willing to function to the last, but it proved impossible to restore a permanent rhythm, and resuscitation was reluctantly abandoned after two hours and a half.

Comments

In this case, we think, repeated tension on the lateral rectus muscle, whilst it was being resected during the closing stages of the operation, stimulated the oculocardiac reflex and initiated several short periods of ventricular fibrillation—as has been described by Sorenson and Gilmore (1956). By great misfortune, pulse-checks never coincided with these probably almost momentary fibrillations. The absence of bleeding in the operation field, observed by the surgeon and mentioned above, is suggestive, although its possible significance was not appreciated at the time. These periods of ventricular fibrillation would bring about repeated short spells of cerebral ischæmia which would progressively damage the cardiac and vasomotor centres and also account for the convulsions. The ischæmia might well have been accentuated by further stimulation of the reflex through pressure on the eye during the application of the bandage.

The convulsions themselves must have added to the damage to the vital centres, causing it to become irreparable, and this would result in complete absence of vasomotor tone and lack of response from the pacemaker. This would render any attempts at permanent resuscitation unavailing, even though the cardiac muscle remained viable.

Only one previous report of a case of cardiac arrest in these circumstances has been found (Sorenson and Gilmore 1956). This suggests that serious consequences from evocation of the oculocardiac reflex is rare. Nevertheless, occurring as it does during the performance of elective surgery in young people, the oculocardiac reflex demands the most widespread attention and the development of techniques to avoid evoking it. Intravenous atropine gr. $^1/_{100}$ has been recommended by Sorenson and Gilmour (1956) for use when irregularities are detected, but this is shutting the stable door when the horse is already out and galloping about. The employment of muscle relaxants with the anæsthetic has been suggested, but this merely reduces the tension required for manipulation of the muscles without blocking the reflex path, and is a somewhat elaborate method in a child patient undergoing a very simple operation. Also, it carries its own risks.

In consultation with our surgeon we now perform a retrobulbar block with 0·5% lignocaine after induction of general anæsthesia. With this technique in use, we have not detected so far, even with the electrocardiograph, any abnormal response to strong tension on the rectus muscles during operation.

Summary

A fatal evocation of Aschner's oculocardiac reflex during anæsthesia for ophthalmic surgery in a child is described.

Retrobulbar block with 0·5% lignocaine is suggested as a preventive technique.

The cooperation and encouragement we have received from Miss Adelaide Carter is gratefully acknowledged, together with her permission to publish the details of the case reported above.

References at foot of next column

PULMONARY ŒDEMA DUE TO SALICYLATE INTOXICATION

K. L. GRANVILLE-GROSSMAN *
M.B. Lond., M.R.C.P.
LATE MEDICAL REGISTRAR

H. G. S. SERGEANT
M.B. Lond.
SENIOR HOUSE-OFFICER

WHITTINGTON HOSPITAL, LONDON, N.19

SALICYLATE intoxication may produce respiratory alkalosis, hypoprothrombinæmia, hæmorrhagic gastritis, acute renal failure, hypokalæmia, or depression of the central nervous system (Robin et al. 1959). Pulmonary complications are less well recognised, but a few cases diagnosed as salicylate-induced pulmonary œdema have been recorded. In these there was evidence of active rheumatic carditis. We here report a case of salicylate intoxication producing pulmonary œdema similar to those previously described but arising in a patient without heart-disease.

Case-report

A man, aged 32, was admitted to Whittington Hospital on July 8, 1958. At first he was unable to give a coherent history, but later we found that since childhood he had had recurrent nasal-sinus infections for which he had taken aspirin on many occasions without ill effect. Otherwise he had been well until 3 or 4 weeks before admission to hospital, when he had experienced a dull aching pain over the left antrum and above the left eye. At first the pain was relieved by aspirin gr. 10–15 per day. After about 10 days, however, the pain worsened and for relief he took gr. 100–200 of aspirin daily. 4 days afterwards tinnitus and deafness developed, followed 4 days later by dyspnœa on exertion. He continued to take aspirin more than gr. 100 daily for 2 more days until the night of July 7, when he became mentally confused.

He was drowsy and confused, with slurred speech. He was afebrile, but sweating profusely. He was breathing deeply at a rate of 26 per min. but was not cyanosed. The pulse-rate was 100 per min. and the blood-pressure 130/70 mm. Hg. Routine examination showed no abnormality, and there was no evidence of congestive cardiac failure.

The urine contained reducing substance (green to 'Clinitest') but no glucose when tested with 'Clinistix'. The ferric-chloride test for salicylate was strongly positive. The hæmoglobin level was 91%, and the white-cell count 22,000 per c.mm., with 95% neutrophils. The prothrombin-time was 20 sec. (normal control 15 sec.). The serum-salicylate level was 44 mg. per 100 ml. The serum-electrolyte levels (mEq. per litre) were: sodium 135, potassium 3·1, chloride 92, and bicarbonate 10. The blood-urea was 50 mg. per 100 ml.

Salicylate intoxication was diagnosed, and the patient was treated by a high fluid intake, sodium bicarbonate 2 g. 8-hourly, crystalline penicillin 1 mega-unit 6-hourly, and vitamin K_1 10 mg. intramuscularly. During the day he became more drowsy and dyspnœic, the respiratory rate rising to 42 per min., and slight central cyanosis appeared. A chest radiograph (fig. 1) showed widespread shadowing in the middle and lower zones of both lung fields, which was thought to be due to pulmonary œdema. The patient was placed in an oxygen tent, and this produced some lessening of the cyanosis and dyspnœa.

* Present address: University College Hospital, Gower Street, London, W.C.1.

DR. MALLINSON, DR. COOMBES: REFERENCES

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There were no abnormal signs in the chest. The jugular venous pressure was not raised, and there was no peripheral œdema. An electrocardiogram was normal.

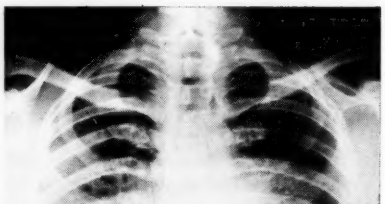

Fig. 1—Chest radiograph on July 8.

Next day (July 9) the serum-salicylate level had fallen to 32 mg. per 100 ml., and the serum-bicarbonate had risen to 24·2 mEq. per litre. As the serum-potassium was only 2·8 mEq. per litre the patient was given potassium chloride 1 g. 8-hourly. During the day his condition deteriorated rapidly, and the blood-pressure and urinary output fell. Aminophylline 0·5 g. intravenously had no effect, but hydrocortisone succinate 100 mg. intravenously produced considerable improvement, the blood-pressure rising from 85/60 to 120/70. Steroids were therefore continued in the form of triamcinolone 8 mg. by mouth every 8 hours. During the next 48 hours the patient's condition continued to improve gradually. On July 10 the serum-salicylate level was 14 mg. per 100 ml., the serum-bicarbonate 29·3 mEq. per litre, and the serum-potassium 3·6 mEq. per litre; a radiograph (fig. 2) showed some increase in the shadowing. On July 14 a further radiograph showed much clearing, and by July 22 (fig. 3) the lung fields were almost clear. He then felt perfectly well, and he was discharged from hospital next day.

Discussion

The clinical and radiological findings suggested a diagnosis of pulmonary œdema. This was assumed to be due to salicylate intoxication, for at no time was there other evidence of congestive failure, or even of heart-disease, and he had taken no drug except aspirin. Similar pulmonary disease due to salicylates has been observed previously.

Reid et al. (1950) reported two patients with rheumatic fever who developed lung lesions, which they ascribed to pulmonary œdema, 6–10 days after starting salicylate therapy. The plasma-volume was raised in both cases, and it was thought that consequent left ventricular failure had resulted in pulmonary œdema.

Phear (1955) described the case of a boy, aged 13, with rheumatic fever, whose chest radiograph showed well-defined bat's wing shadowing 6 days after treatment with sodium salicylate and sodium bicarbonate was started. Examination at this time revealed only a few rales at one lung base. Phear ascribed the lung lesions to pulmonary œdema due to a high-sodium intake (as salicylate and bicarbonate), and he therefore changed the treatment to acetylsalicylic acid, digitalis, mersalyl, and a low-sodium diet. On this regime the patient gradually improved.

Sutcliffe (1955) reported the case of a 13-year-old girl with rheumatic fever, who was treated with salicylates in three separate courses. After 6–7 days' treatment on each occasion, fever, dyspnœa, and cyanosis developed, with widespread shadowing throughout the lung fields suggestive of pulmonary œdema. The symptoms and pulmonary shadowing gradually disappeared when the drug was stopped. This patient also showed evidence of "systemic capillary damage—the development of purpura and a positive Hess's capillary fragility test", but she did not have the usual symptoms of salicylate overdosage. Sutcliffe concluded that these episodes, apparently of pulmonary œdema, were possibly due to an increase in plasma-volume combined with pulmonary capillary damage arising from a sensitivity reaction to salicylates.

Thus, three different mechanisms have been suggested to account for pulmonary œdema in patients taking salicylates. Phear's suggestion (1955) that the high-sodium intake rather than the salicylates might be responsible, clearly does not explain our case, where only acetylsalicylic acid was taken. Sutcliffe's view (1955) that the pulmonary œdema might be due in part to a sensitivity reaction could apply in our patient, who showed improvement after hydrocortisone was given. On the other hand, he showed no evidence of systemic capillary damage, and the response to hydrocortisone may have been non-specific. Reid et al. (1950) demonstrated that salicylates enhance protein breakdown and increase the plasma-volume. They thought that the rise in plasma-volume, which they regard as secondary to increased protein breakdown, produced left ventricular failure and subsequently pulmonary œdema. A fourth possibility is suggested by the experiments of Hetzel et al. (1959) which showed that when salicylates are given to healthy subjects sodium and water are retained. Thus sodium retention caused by the continued ingestion of large quantities of salicylates may have been responsible for pulmonary œdema in all the cases cited. If this were so, a high-sodium intake or the presence of heart-disease would predispose to pulmonary œdema, and treatment by sodium restriction, diuretics, or venesection would tend to relieve it. In fact Phear's patient responded to digitalis, mersalyl, and a low-sodium diet while still taking salicylates in the form of acetylsalicylic acid. In the cases of Reid et al. venesection gave immediate benefit. The improvement in Sutcliffe's case and in our own seemed to be due to withdrawal of the drug.

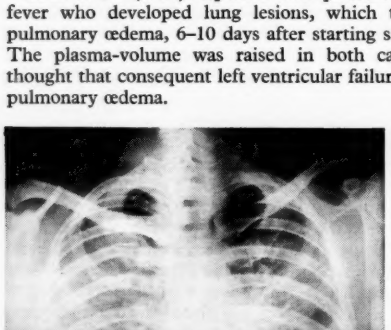

Fig. 2—Chest radiograph on July 10.

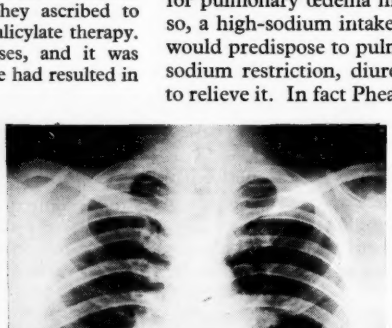

Fig. 3—Chest radiograph on July 22.

Reid et al. (1950), Sutcliffe (1955), and Phear (1955) all mentioned the resemblance of their cases to "rheumatic" pneumonia. But descriptions of this condition vary so much that it is impossible to define a specific clinical syndrome (Brown et al. 1958). The radiographic appearance

is frequently indistinguishable from that of pulmonary œdema (Goldring et al. 1958). Further, the contrast between the paucity of physical signs and the considerable radiographic changes is often as striking in cases of rheumatic pneumonia (Brown et al. 1958, Lustok and Kuzma 1956) as it was in Phear's case and in ours. Sutcliffe suggested that some cases of "rheumatic" pneumonia which have been reported may in fact have been examples of salicylate-induced pulmonary œdema. Our case strongly supports this view, although it differs from those previously described in showing no evidence of rheumatic fever. Hence it was not necessary to consider the diagnosis of rheumatic pneumonia.

Salicylate-induced pulmonary œdema seems to arise most often in rheumatic fever. Therefore when pulmonary complications appear in such cases which are treated with salicylates, pulmonary œdema due to salicylates should be considered as an alternative diagnosis to rheumatic pneumonia.

Summary

Salicylate intoxication with pulmonary œdema is described in a patient without heart-disease.

The most likely mechanism is thought to be sodium retention.

Salicylate-induced pulmonary œdema is difficult to distinguish from "rheumatic" pneumonia, and both conditions should be considered when pulmonary complications appear in rheumatic fever.

We wish to thank Dr. Arnold Bloom, under whose care the patient was treated, for permission to publish this account; and Dr. Gordon Osborne for his interest and encouragement.

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Preliminary Communication

THE DEOXYRIBONUCLEIC ACID CONTENT OF THE NUCLEI OF LEUKÆMIC LEUCOCYTES

THE deoxyribonucleic acid (D.N.A.) content (amount per cell) of the resting nuclei of cells of all of the tissues of any one species is a constant related to the number of chromosomes in these cells.[1] If the nuclei are not resting but are synthesising, or have synthesised, D.N.A., prior to cell division then they contain an increased amount of D.N.A.[2 3] This synthesis of D.N.A. during interphase and the equal partition of the accumulated D.N.A. into the two chromosome sets in the metaphase of cell division is a faithfully replicated process in normal actively dividing tissue.[4] If the cells contain an increased number of chromosomes (polyploidy) or an increased number of chromosome threads (polyteny) then the nuclei will show a related increase in D.N.A. content.[1] Biochemical analysis of tissues to determine the mean amount of D.N.A. which they contain will give a constant figure if the tissue is resting. If the tissue is regenerating and contains a considerable number of cells which are polyploid or polytene then the mean D.N.A. content will rise; the extent of the rise depending upon the number of cells showing these changes and the degree of change within the cells. Biochemical analysis will give no information about which of these changes is causing the rise. Quantitative cytochemical analysis of single cells will, however, reveal these changes since it allows one to study the pattern of distribution around the mean value.

In many malignant neoplasms the chromosome number of the cells has changed.[5 6] This change is reflected in an alteration in the pattern of distribution of D.N.A., which has been detected by cytophotometry.[7 8] The change is usually seen as a rise in the modal value and a broadening of the distribution.

Because of technical difficulties it was previously impossible to use cytophotometry for investigation of the rather dense and irregular nuclei of leucocytes and thus detailed study of leukæmic leucocytes was prevented. Developments in technique have however overcome these difficulties.[9 10] Using these techniques we found in a previous investigation [11] that the D.N.A. content of the nuclei of leucocytes in the peripheral blood of patients with leukæmia, of various types, showed a pattern of distribution similar to that of the nuclei of normal cells in a tissue show-

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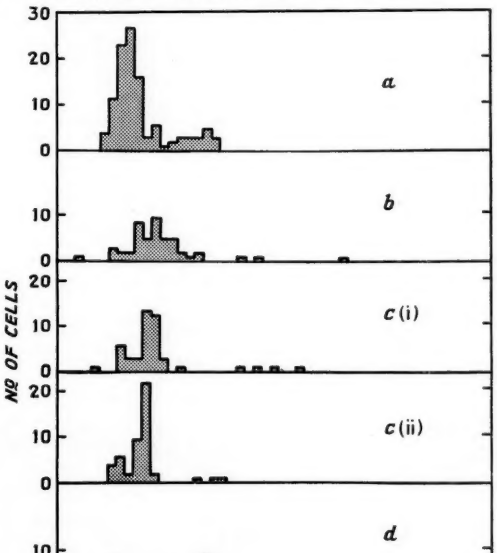


Distribution of D.N.A. in the nuclei of the cell population. The pattern found in the 27 samples reported in table I is given in *a*. Those for the samples reported in table II are given in *b–e* The absorbance is a measure of the absolute amount of D.N.A. in any one cell.

TABLE I—SOURCE OF SAMPLES SHOWING A D.N.A. DISTRIBUTION CHARACTERISTIC OF NORMAL DIVIDING TISSUE (FIG. A)

Type of sample	No. of cases	Diagnosis
Blood	7	Chronic myeloid leukæmia
	2	Chronic lymphatic leukæmia
	1	Acute myeloid leukæmia
	1	Acute lymphatic leukæmia
	1	Acute monocytic leukæmia*†
	1	Acute unclassified leukæmia*‡
	3	Reticulosarcoma†
	1	Atypical mononucleosis
	1	Subacute lymphatic leukæmia‡
Bone-marrow	2	Chronic myeloid leukæmia
	1	Chronic lymphatic leukæmia
	1	Acute unclassified leukæmia*‡
	1	Reticulosarcoma†
	1	Acute monocytic leukæmia*†
Lymph-node	1	Subacute lymphatic leukæmia
	1	Acute monocytic leukæmia‡
	1	Follicular lymphoblastoma

* Blood and bone-marrow from the same patient.
† From one case of reticulosarcoma the blood and bone-marrow showed distributions typical of normal dividing tissue whereas the lymph-node showed the distribution reported in table II.
‡ Bone-marrow from this patient showed the distribution reported in table II.

TABLE II—SOURCE OF SAMPLES SHOWING A D.N.A. DISTRIBUTION CHARACTERISTIC OF ABNORMAL DIVIDING TISSUE

Type of sample	No. of cases	Diagnosis	Distribution
Bone-marrow	1	Subacute lymphatic leukæmia	Fig. b*
	1	Subacute lymphatic leukæmia	Fig. c(i)†
	1	Acute monocytic leukæmia	Fig. d‡
Lymph-node	1	Subacute lymphatic leukæmia	Fig. c(ii)†
	1	Reticulosarcoma	Fig. e§

* The peripheral blood of this patient showed a distribution typical of normal dividing tissue.
† Bone-marrow and lymph-node from the same patient.
‡ A lymph-node of this patient showed a distribution typical of normal dividing tissue.
§ The peripheral blood and bone-marrow of this patient showed distributions typical of normal dividing tissues.

ing active cellular division. This finding was of some significance since it was suggested that leukæmic cells in this respect differed from many neoplastic cells. We have since extended our investigations, using the integrating microdensitometer, to measure the amount of Feulgen-stained D.N.A. in the nuclei of leucocytes of peripheral blood, bone-marrow, and lymph-nodes in cases of leukæmia and related diseases. The technique used was the same as that already described by us.[11] In the investigation reported here we examined the 32 samples listed in tables I and II. 10 normal marrows and lymph-nodes were also examined.

In all these samples the distribution of D.N.A. in the cell population was similar to that of either a normal resting or an actively dividing tissue (table I, fig. a) except for the samples indicated in table II and illustrated in fig. b–e, 3 from bone-marrow, 2 from lymph-nodes. It can be seen that in these cases there is some alteration in the pattern of D.N.A. replication. This alteration is similar to that reported by Leuchtenberger et al.[7] and Atkin and Richards [8] for many malignant neoplasms. It is interesting, however, that only in a few of the samples (4 out of 32) reported here has the alteration been detected. The alteration is interpreted as indicating a change in the chromosomal quantity of D.N.A. either because of an increase of the amount of D.N.A. per chromosome or an increase in the number of chromosomes.

It has been reported by Ford et al.[12] that the bone-marrow of 1 case of leukæmia, in a series of 3, contained cells with a chromosome number of 44 instead of the normal number of 46 and that in addition a few of the cells contained 88 chromosomes. Baikie et al.[13] reported 13 cases of leukæmia in which some of the cells in the bone-marrow of 2 acute leukæmias were found to have up to 50 chromosomes and 2 other cases had chromosomes which were altered in appearance but not in number.

Our finding in a minority of cases of an abnormal pattern of D.N.A. distribution in the nuclei of cells in the leucocyte-forming tissues, but not in the nuclei of cells in the peripheral blood, may well be due to an alteration in the chromosome number. The number of cases investigated by either technique is still too small to permit any generalisation about the results, but it is interesting to note that no alteration in the chromosome number or D.N.A. content has been reported in cases of either chronic myeloid or chronic lymphatic leukæmia. The actual relationship between these changes in the marrow and lymph-nodes and the rate of progress of the disease is of considerable interest and is at present being investigated. The data will be published in detail at a later date.

12. Ford, C. E., Jacobs, P. A., Lajtha, L. G. *Nature, Lond.* 1958, **181**, 1565.
13. Baikie, A. G., Brown, W. M. C., Jacobs, P. A., Milne, J. S. *Lancet*, 1959, ii, 425.

SUMMARY

In 2 cases of subacute lymphatic leukæmia, 1 of acute monocytic leukæmia, and 1 of reticulosarcoma, the pattern of distribution of deoxyribonucleic acid in the nuclei of the cell population of the bone-marrow and of lymph-nodes was similar to that in the nuclei of the cells of many neoplasms.

The deoxyribonucleic acid content of the nuclei of cells from the peripheral blood, bone-marrow, and lymph-nodes of several other cases of leukæmia and related diseases was found to be distributed in a manner identical with the distribution in the nuclei of cells in a normal tissue.

We are grateful to Prof. R. C. Garry for his encouragement and his enthusiasm in providing facilities. One of us (S. J. W.) is in receipt of a Medical Research Council scholarship for training in research methods. The construction of the integrating microdensitometer was financed by the M.R.C.

We also wish to thank several physicians in the Glasgow area for allowing us access to their patients.

A. J. HALE*
M.B., PH.D., D.SC. Glasg.
SYLVIA J. WILSON
B.A. Mount Holyoke

Institute of Physiology, The University, Glasgow

* Present address: Division of Pathology, Imperial Cancer Research Fund, Lincoln's Inn Fields, London, W.C.2.

New Inventions

ELECTRONIC MONITORING APPARATUS FOR COIL KIDNEY

EMACK was designed in the medical electronics laboratory of No. 248 Maintenance Unit, R.A.F., Chessington, for use with the Kolff disposable twin-coil artificial kidney 'Travenol' in the Renal Unit at Princess Mary's Royal Air Force Hospital, Halton.

The monitor was incorporated in the kidney to ensure rapid detection of faults and to reduce strain in the operator. A dialysis, with preparation, takes nearly nine hours, the actual dialysing time being usually six hours.

The functions of EMACK are: (1) Measurement of the rate of blood-flow through the kidney. (2) Audible and visual indication when the flow-rate differs by more than $\pm$ 10% from a previously selected rate. (3) Indication of the temperature of the dialysing fluid. (4) Control of tank temperature. (5) Monitoring of the level of the dialysing fluid and automatic cut-out of the tank heaters when the fluid falls below a safe level. (6) Indication of the pressure in the venous (outflow) circuit.

The following description is necessarily brief: a more complete report giving circuit and constructional details is in preparation.[1]

1. Brennand, R. T.R.D.S. R.A.F. Technical Report (in course of preparation).

An electromagnetic induction flow-meter [2–4] is employed, and has proved most satisfactory. The blood flows through a robust detachable head unit (see figure), cast in Araldite F. This may be autoclaved and can be inserted into the outflow circuit in less than thirty seconds. The small voltages from the head unit are amplified by a three-stage double triode differential amplifier, and rectified, and the resulting direct-current output signal is fed to a panel-mounted meter having a linear scale calibrated from 0 to 500 ml. per min. A switch permits introduction of an additional range of 0–1000 ml. per min. The direct-current output signal is also fed into a second differential amplifier which continuously compares the direct-current flow signal with a stabilised demand voltage. The difference, or error signal, is employed to operate a flashing light and to trigger an audio-oscillator, so as to produce an audible interrupted signal. The oscillation frequency is high or low depending on the direction of the error signal. Thus a higher pitched "beep beep" means that the kidney blood-flow has exceeded the desired figure.

The temperature of the dialysing fluid is monitored by a direct-reading thermistor thermometer scaled from 0 to 50°C. At present, the tank temperature is controlled by a conventional thermostat, but we think that this could well be replaced by the thermistor probe, which would then perform a dual function. The fluid level is monitored by means of a probe so arranged that the fluid produces a low resistance across the tuned circuit of an audio-oscillator. When the fluid level in the tank falls, uncovering the probe, the oscillator operates a relay which disconnects the tank heaters.

EMACK has proved very reliable in operation and has been used for sixty dialyses. Together with other modifications, it enables two persons (a medical officer and a nursing sister) to carry out the complete dialysing operation, and is effective in reducing the stress of constant observation on the operator.

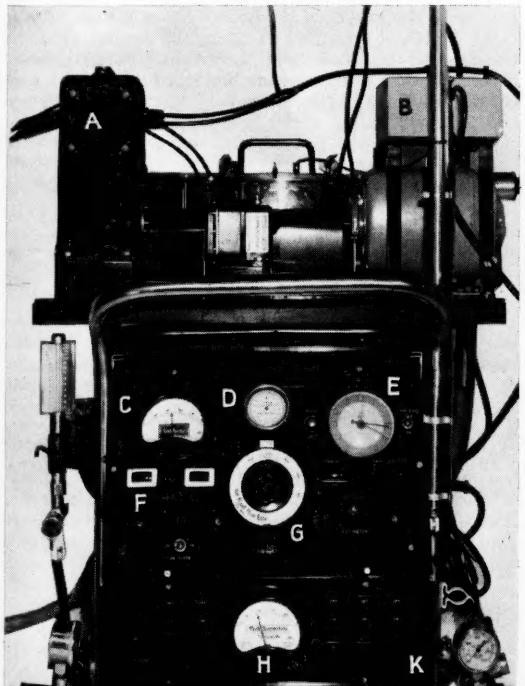
Disorganisation of the inflow (arterial) side of the extracorporeal circulation—e.g., a broken connection, a kinked catheter, or a burst in the coil—is signalled in about four seconds. Disruption of the outflow (venous) circuit, into which the flow-meter head is connected, is signalled instantly.

We wish to thank the Director-General of Medical Services of the Royal Air Force for permission to publish, Group Captain R. C. Jackson for his advice and encouragement, and the various members of the technical repair and development section, No. 248 Maintenance Unit, who constructed the apparatus. We are also indebted to Mr. P. Styles of St. Thomas's Hospital for much valuable information on the design of the flow-meter head.

Medical Electronics Laboratory,
No. 248 Maintenance Unit,
Royal Air Force,
Chessington, Surrey
R. BRENNAND
A.M.BRIT.I.R.E.

Renal Unit, Princess Mary's
Royal Air Force Hospital,
Halton, Bucks
N. V. BUNKER
M.B. Cantab.

2. Katz, L. N., Jochim, K. *in* Medical Physics; p. 377. Chicago, 1944.
3. Kolin, A. *Rev. sci. instrum.* 1956, **27**, 707.
4. Wyatt, D. G. *in* Proceedings of the 2nd International Conference on Medical Electronics (to be published).



General view of the artificial kidney showing the monitoring apparatus and other modifications.

(A) Blood pump. (B) Flow-meter head unit and magnet block. (C) Flow-rate meter. (D) Manometer. (E) Alarm clock. (F) Warning lights. (G) Flow-rate selector dial. (H) Dialysing fluid temperature. (K) Pump switches.

Reviews of Books

Cancer

Vols. V and VI. Editor: RONALD W. RAVEN, O.B.E., F.R.C.S., surgeon, Royal Marsden Hospital and the French Hospital. London: Butterworth. 1959. Vol. v, pp. 425; vol. VI, pp. 517. 85*s.* each.

THE fifth and sixth volumes of this system of cancer complete the work, except for a final index. The first four volumes we reviewed [1 2] in 1958 and 1959. The whole work has thus appeared in the space of two years, which is certainly a matter for congratulation to the editor and authors.

Volume V is entirely devoted to radiotherapy, rather more than a third being concerned with the general principles governing radiations and their uses, and the remainder with the treatment of cancer in each anatomical site or system. Thus the pattern used in earlier volumes for the pathology and surgical treatment of cancer is also used for radiotherapy. A laudable attempt is made to state the relative merits of radiotherapy and surgery or a combination of the two, and to admit differences of opinion where they exist; but the reader with little clinical experience may be left in doubt about how much benefit the patient can expect from the methods of treatment advocated.

The first part of volume VI is concerned with chemotherapy and gives an excellent summary of the present position concerning the theory and use of biological alkylating agents, anti-metabolites, and hormone administration and withdrawal—a subject which has raised great hopes and produced many disappointments. The second part of volume VI is a collection of articles classed as the public health and nursing aspects of cancer, probably the least essential part of the work.

Each volume may be purchased separately, but undoubtedly many individuals and organisations will want to have the complete work, even at a cost of over £25 for the set. What will they have obtained? First, a good insight into the magnitude of the effort being put into worldwide investigations of the mechanisms of cancer induction and of therapeutic trials; and secondly, a survey of modern views of the pathology of human tumours, with some information about geographical variations in site incidence. No attempt is made to conceive new ideas or to wander far into the path of speculation, and these books will therefore mainly act as reference works to the general rather than the specialised reader.

1. *Lancet*, 1958, i, 1003.
2. *ibid.* 1959, i, 291.

Variations on a Theme by Sydenham: Smallpox

P. B. WILKINSON, M.R.C.P. Bristol: John Wright. 1959. Pp. 76. 17*s*. 6*d*.

THIS is indeed such a book as Thomas Sydenham might have written if he had lived after Jenner. It is an account of the signs and symptoms of smallpox seen in 810 patients during an epidemic in Hong Kong in 1937–38. The author's views on the pathology of the disease may be correct but he makes no attempt to support them by authority or by evidence from the laboratory. He tells what he saw and draws some conclusions about diagnosis and prognosis. He suggests a not unreasonable explanation which might be a useful start for fresh laboratory work. His descriptions of the objective phenomena of disease are far better than we are accustomed to in these days. Not only does he present a picture which we can see clearly—even without the many excellent photographs by Mr. Lo Fuk—but also his individual patients are defined characters like those of Sir William Osler or Dr. George Day.

The modern doctor will probably glance at the pictures and neglect the text when he finds that there are no figures, no tables, and no references. If he never sees a patient with smallpox he will harm no-one but himself. Otherwise a time will come when he will find this book valuable and comforting.

Klinik und Praxis der Urologie

Prof. Dr. WERNER STAEHLER, urological department, Chirurgischen Universitatsklinik, Tubingen. Vol. 1. Pp. 892. Vol. 2. Pp. 863. Stuttgart: Georg Thieme. 1959. DM 480. 2 vols.

THE scope of this specialty has become so great and its advances so numerous that it is a rare feat for such a comprehensive and up-to-date treatise to be compiled by a single individual. In this respect the work emphasises an advantage of the Continental system whereby the formation of a special department or clinic attracts much material and provides exceptional facilities for investigation and management. Drawing on this wide experience and aided by many excellent illustrations, Professor Staehler gives an all-embracing study of urology, worthy of inclusion in all reference libraries dealing with this branch of surgery.

The matter is arranged broadly on ætiological lines, thus allowing ready comparison of similar types of disease in all parts of the genitourinary tract, and providing an integrated account of such subjects as urinary infection and lithiasis Most of volume 1 deals with the essential clinical, pathological, and radiological features, and is well sustained by suitable references and appropriate illustrations. Outstanding are the sections on urinary lithiasis, and, although nowadays partly outmoded, on urogenital tuberculosis. Volume 2 emphasises the importance of medical urology, with a detailed study of anuria and a comprehensive chapter on nephritis. Further descriptions of such varied subjects as urinary fistula, parasitic disease, and male infertility are followed by a detailed review of methods of investigating urological disease and its surgical treatment. Not least in importance is the exhaustive index and a wide range of references at the end of each section. The publishers have maintained a high standard in the production of two imposing volumes.

Medical Discoveries: Who and When

J. E. SCHMIDT, PH.B.S., M.D., LITT.D. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959. Pp. 555. 118*s*.

EVEN Samuel Johnson found many pitfalls in the path of a lexicographer, and the author of this new dictionary has rediscovered several of them. His book is a laudable attempt to catalogue the names, dates, nationalities, and professions of the earliest known observers of thousands of phenomena in medicine and the related sciences; and, understandably, the arrangement of the entries was a formidable problem. In general an eponymous sequence has been avoided, and the various discoveries are listed under the appropriate principal nouns, in alphabetical order. Thus Colles' fracture is described under "Radius, fracture of". Unfortunately this system has not been used consistently (e.g., Gram's stain is found as such, and not under "Stain" or "Bacteria"). This makes the book rather difficult to use, particularly for a reader who does not know the exact nature of the discovery he is checking. It is frustrating to find no mention of Perthes' disease under Perthes, femur, hip, or even pseudo-tuberculosis and coxalgia, and a student might be excused for renouncing his search before turning to "Osteochondritis".

In a preface Dr. Schmidt says that the search for the occupation or profession of each of his subjects "paid off with its own brand of surprises": some readers will be surprised to see Astley Cooper called an "English physician"; and Krukenberg, who described mucus-cell carcinoma of the ovary, was not a pathologist but an ophthalmologist.

This book contains an enormous amount of information not readily obtainable elsewhere—the name, for instance, of the first man to catheterise the eustachian tube and the date of the introduction of Seidlitz powders. But medical historians will regret that not a single bibliographical reference is appended to the entries.

Readings in Psychoanalytic Psychology

Editor: MORTON LEVITT, PH.D., associate professor of psychiatry and assistant dean, Wayne State University College of Medicine, Detroit, Michigan. London: Staples Press. 1959. Pp. 413. 70*s*.

THIS book consists of chapters contributed by 23 psychoanalysts, mostly of the American school, on a wide range of psychoanalytic theory and practice: 14 chapters are original contributions, 12 having been previously published elsewhere. Inevitably, the quality of the book is uneven, some chapters being exhaustive treatment of theory, and others protracted case-histories to illustrate a theoretical concept. British psychoanalytic contributions are limited to papers by Edward Glover and Willie Hoffer, so the book is strikingly American and Viennese in orientation. Among the more valuable chapters are Margaret E. Fries' review of the literature on the latency period, one dealing with transference by Phyllis Greenacre, and one by the only non-analyst, Lionel Trilling, on Freud and literature.

Mostly Murder

Sir SYDNEY SMITH, C.B.E., M.D., F.R.C.P.E. London: George G. Harrap. 1959. Pp. 318. 21*s*.

THE title of this book is not exactly a misnomer—for, certainly, it is principally concerned with felonious killings. But these are murders considered with a precision, and an elegance of style, which give the author more in common with De Quincey than with most of those writers for whom murder is a stock-in-trade.

In 1917 Sir Sydney was appointed to control the medico-legal section of the Ministry of Justice in Cairo, and his acquaintance with murder, other than as a fine art, may be held to date from then. (In Egypt at that time "there were about a thousand cases of murder and as many attempted murders every year.") The first half of his unusual biography is devoted to a few of the problems he encountered in a country which had, until he developed them, very few facilities for the scientific investigation of crime. His pioneer studies in forensic ballistics are particularly noteworthy, since the identification by him, in 1925, of the revolver with which the Sirdar had been assassinated, established throughout the world the methods he had used.

The later chapters describe his activities, as professor of forensic medicine at Edinburgh, in the investigation of many cases of more recent times. On several occasions Sir Sydney found himself opposing the late Sir Bernard Spilsbury, and he speaks critically (as others have done) of Spilsbury's reputation for infallibility and of his intransigence in the face of opinions contrary to his own. The book is abundantly illustrated with a series of remarkable photographs.

THE LANCET

LONDON 12 MARCH 1960

Resistant Tubercle Bacilli

THROUGH failures of chemotherapy the population of tubercle bacilli in a community might change in pattern until eventually all new infections were produced by bacilli resistant to one or more of the usual drugs. This danger has been recognised since the start of tuberculosis chemotherapy; but the extent of the change so far in different countries is almost unknown. In 1955–56 the Medical Research Council [1] carried out a sample survey in Great Britain of the drug sensitivity of strains of bacilli isolated from newly diagnosed patients. 5·1% of 974 cultures were resistant to one or more of the three commonly used drugs—2·3% to streptomycin, 2·2% to *p*-aminosalicylic acid (P.A.S.), and 0·7% to isoniazid. There were considerable differences between the age-groups; of women with newly diagnosed tuberculosis 9·3% aged 15–34 had resistant cultures, but of those over the age of 34 only 4·9%. The survey should certainly be repeated. An international inquiry [2] suggests that the proportion of "primarily" resistant cultures in the various countries surveyed may be slightly higher than 5%; and there is now evidence of an alarming increase of resistant strains in East Africa [3] between 1953 and 1958.

In this period the Medical Research Council carried out a series of chemotherapy trials in Uganda, Kenya, and Tanganyika. The same types of patients were admitted to each—previously untreated patients with acute pulmonary tuberculosis affecting both lungs. In the first trial in 1953–55, of 56 patients in whom sensitivity tests of cultures were obtained before treatment, none had cultures resistant to isoniazid or P.A.S. But in a trial begun in 1956 8% had isoniazid-resistant and 3% P.A.S.-resistant cultures; and in 1957 the proportions had risen to 16% and 13%. Resistant cultures were found in all three countries during the period: they amounted to 10% of the total in Uganda, to 6–9% in Kenya, and to 9–27% in Tanganyika. The observed prevalence of "initial" resistance is probably less than the true prevalence throughout the population, for the patients admitted to these trials were presumed from their histories to have had no previous chemotherapy. In fact, however, some of them later admitted to previous treatment; so, while underestimating the extent of bacterial resistance in all patients coming for treatment, the study probably overestimates the extent of primary infection with resistant strains. Although these findings have not the precision and significance of the sample survey in Great Britain, there is no reasonable doubt that they indicate a rapid change in the population of tubercle bacilli in these countries. A similar change may have taken place elsewhere; and its extent may vary with the ease with which anti-tuberculosis drugs can be obtained from non-medical sources, and the standard of medical prescription and supervision. In some areas the prevalence of resistance may, of course, be lower than that found in East Africa: in an investigation in Madras in 1956–57 [4] infection with isoniazid-resistant strains was thought to have occurred in only 3·6% of the patients, with P.A.S.-resistant strains in 2·6%, and with streptomycin-resistant strains in 2·2%.

The rapid increase of resistant strains in East Africa is alarming; but the implications are not straightforward. What, for instance, is the clinical significance of initially resistant cultures? Will all patients who have them fail to respond to treatment with the commonly used isoniazid-P.A.S. regime? There is at present no report of the fate of the patients with initially resistant cultures in the East African studies. In the Madras investigation 9 patients had isoniazid-resistant cultures before treatment with P.A.S. and isoniazid was begun. 2 admitted to having had previous chemotherapy: they fared badly; both remained sputum-positive throughout the year's treatment, with P.A.S.-resistant strains emerging. 7 were regarded as having been infected with isoniazid-resistant strains: 3 did well, being sputum-negative at the end of a year; 3 did badly, and 1 of these died after only three weeks' treatment; the 7th patient got worse and treatment was changed, with satisfactory results. 6 patients had P.A.S.-resistant cultures before treatment. 1 had had previous treatment; P.A.S. was discontinued because of hypersensitivity to it, and the patient did well under streptomycin and isoniazid therapy. 5 were considered to have been infected by P.A.S.-resistant strains; 3 fared well and became sputum-negative; 1 did badly, and isoniazid-resistant strains emerged; and in the remaining patient chemotherapy was changed, with good effect. Thus, of the whole group of 12 patients probably infected by resistant strains, 6 became non-infectious during a year's treatment with two drugs, to one of which the pre-treatment culture was resistant. On the other hand, both patients with cultures isoniazid-resistant as a result of previous chemotherapy did badly. Apparently resistance of the organisms to isoniazid or P.A.S. materially reduces, but does not abolish, the chance of treatment being effective.

The different responses in such patients could be explained by differences between them in the resistance and homogeneity of the bacterial populations and the

1. Fox, W., Wiener, A., Mitchison, D. A., Selkon, J. B., Sutherland, I. *Tubercle, Lond.* 1957, **38**, 71.
2. Crofton, J. W., Rist, N. *Bull. Un. int. Tuberc.* In the press (cited by J. Crofton. *Brit. med. Bull.* 1960, **16**, 61).
3. Pepys, J., Mitchison, D. A., Kinsley, B. J. *Tubercle, Lond.* 1960, **41**, 32.
4. Tuberculosis Chemotherapy Centre, Madras. *Bull. World Hlth Org.* 1959, **21**, 51.

ability of the host to deal unaided with a proportion of his bacterial parasites. Judging from the Madras experience, if 100 previously untreated patients with acute cavitating lesions contains 10 with resistant strains and all are treated with P.A.S. and isoniazid, about 90% of the 90 with sensitive cultures and 50% of the 10 with resistant cultures—86 in all—will become non-infectious. Even if the proportion with resistant cultures rose to 50%, the proportion becoming non-infectious with this "standard" treatment might still be about 70%—a worth-while contribution from unselective chemotherapy, both for the individual patients and for the public. Sensitivity testing is impracticable on a large scale in many—probably in most—parts of the world. Nor can streptomycin, P.A.S., and isoniazid be freely used together in all newly diagnosed patients with cavities; in some circumstances the cost of even one drug is too high. Where P.A.S. and isoniazid can be used, but without guidance from sensitivity tests, it seems likely that they will continue to be effective in a high proportion of cases for many years to come. Isoniazid is being widely used by itself, because of its cheapness and simplicity of administration. Its widespread use, even in large doses, is likely to lead to increasing isoniazid-resistance in the bacterial population; but little is known about its efficacy in patients with initially isoniazid-resistant cultures. Even in countries with declining infection and high standards of treatment through economic and social conditions, the time may come when all the residual tuberculosis is caused by bacillary strains insensitive to the commonly used drugs. Every effort to avoid the breeding of resistant strains should be made everywhere within the limits imposed by shortage of money and staff.

It might be maintained that in tuberculosis the dangers of bacterial resistance are so great that the drugs should never be used on a large scale except in the known effective combinations and regimens. Such an opinion is vulnerable. Admittedly, to treat patients with too small doses of drugs for too short a time endangers the healthy and hastens the time when none of the present drugs will be effective. But should a patient be denied the chance of continuing to live because of an unmeasurable risk of harming the community? There seems to be no humane reason for authoritarian withholding of the means of treatment; but there are sound reasons for regulating the use of these means and encouraging their effective application. To stop the sale of anti-tuberculosis drugs except where these have been medically prescribed would help. Furthermore, Governments could try to find more money to supply more drugs cheaply or freely, in order to make the "black market" unprofitable. The rise in the prevalence of resistant tubercle bacilli in some countries can probably be attributed rather to lack of money than to lack of medical skill—though doctors must keep constantly in mind the essentials of effective treatment. The reported rise in East Africa has happened in three countries that are the responsibility of Great Britain; and we must bear some of the blame.

More Speed, Less Haste

IN craftwork changes are not easily introduced, since skills, once learnt, call for little thought; technique becomes the epitome of the craftsman's endeavour. Thus speed in operating, developed to reduce the period of endurance in the pre-anæsthetic era, in many centres did not disappear until long after the need had gone. Such proud and admiring boasts as that old Sawbones could remove a gallbladder in seven minutes dead are still to be heard occasionally at surgical gatherings, though what was necessary speed in the 19th century can only be rated as excessive haste today when fluid restoration and modern anæsthesia have relieved surgeons of the need to keep one eye on the clock.

Paradoxically the reverse situation also exists. A more leisurely approach came first in Europe from KOCHER, though his influence on his contemporaries in this respect was surprisingly small (his pupil, ROUX, maintained an interest in speed throughout his life). Very different was the influence of HALSTED, whose hegemony still flourishes. HALSTED's pupil, HARVEY CUSHING, spread the gospel; and there have been many disciples. CARTER [1] calculated that of the 238 surgeons who were either CUSHING's residents or assistant residents, or residents of the next generation influenced by the first, 37 had become professors, 14 clinical professors, 18 associate professors, 14 clinical associate professors, 17 assistant professors, 16 clinical assistant professors, and 23 instructors. With such a following small wonder that to some eyes [2] North American surgery sometimes seems dilatory.

Does the duration of an operation really matter? MCNEER and PACK [3] demonstrated a relationship between the duration of operation and mortality in cases submitted to total gastrectomy in the years 1931–52. Such a correlation should be regarded with reserve, since many factors unrevealed by the analysis must have some influence (for instance, the longer operating-time sometimes required for an advanced lesion); but the analysis did show that long operating-time was associated with an increase in cardiorespiratory complications and, surprisingly, of anastomotic dehiscence (which developed in 77% of cases when the operation lasted for more than six hours)—a complication which MCNEER and PACK ascribe to fatigue in the surgical team.

There are reasons for developing again the ability to complete an operation, or stages within an operation, at speed; for speed in itself need be neither damaging nor dangerous. Sometimes speed is essential: during insertion of an arterial graft without the aid of an oxygenator pump [4] the limb is in jeopardy; and in cardiac surgery with such a pump the less time spent with the heart stopped the better. Furthermore in these days of sepsis the less the tissues are exposed to possible contamination the better. OGILVIE [2] has enumerated further reasons for reasonable dispatch in general surgery.

1. Carter, B. N. *Surgery*, 1952, **32**, 518.
2. Ogilvie, H. *Arch. Surg.* 1950, **61**, 7.
3. McNeer, G., Pack, G. T. *Cancer*, 1954, **7**, 1010.
4. Ashton, F., Rains, A. J. H. *Lancet*, 1959, i, 7114.

In many operations there is a time for unhurried deliberation and a time for rapidity; the newcomer to surgery should strive to attain not one or the other, but both. Haste is the weakness of the tiro, speed the achievement of the experienced. But the experienced surgeon cannot work at speed throughout a long operation; like an oarsman he learns to take his rest between the strokes. By never forgetting the objective of the operation he makes a direct approach without unnecessary manœuvre but with a self-critical study of time and motion. Thus some of the most careful surgeons are also the most rapid; and not a few relieve their inner tension by soliloquy at the same time—a habit NISSEN considers retarding. There remains the matter of judgment, of choosing the right moment to change gear: a facility, FONIO tells us, enjoyed by the father of leisurely operating—KOCHER himself.

Growth and Stability in the Newborn

THE Bible, mythology, history, and even modern fiction abound with strange tales of infants abandoned on rocks, in the desert, at sea, and in forests, to be nursed into childhood by wolves, birds, apes, and giants. Not all of them become founders of city-empires or kings of the jungle, but even sceptics must concede that newborn babies are singularly well fitted to survive such rigours. Their survival, as indeed our own, depends on a series of physical and chemical "steady states"; and the self-regulating systems which maintain them are already in a high state of efficiency at birth. It is not always realised that the fœtus and its adnexa create their own large volumes of extracellular fluid (gradually reducing it in those parts which are destined for an independent extrauterine existence), that they preserve the composition of the amniotic and allantoic fluid, and that they regulate the volume, aminoacid level, and immune-body content of the placental blood-flow. Birth involves no break in this: indeed, many fœtal steady states—such as the high blood-fructose and serum-creatinine of some ungulate fœtuses or the aminoacid excretion pattern in babies—are carried forward into the first weeks or months of neonatal existence. Nevertheless, if in some respects the hardiness of the newborn animal or human infant is astounding, many noxious agents which could do no harm to the fully developed organism can destroy or permanently damage it. The newborn is not just a little adult: its stabilising mechanisms can function only if certain external conditions are fulfilled.

In a wide but penetrating survey of neonatal physiology MCCANCE [1] observes that birth is a major upheaval "mainly for what may be described as the supply services and sewage department"; and of these two the second is perhaps the more puzzling. There is naturally a temptation to compare the renal function of the newborn with that of an adult; and in some respects such comparisons are valid and revealing. (Thus MCCANCE and WIDDOWSON [2] have shown that the kidneys of the newborn cannot raise the osmolar concentration of urine as effectively as the kidneys of an adult.) Other functions, however, such as glomerular filtration and urea-clearance, cannot be fairly expressed unless the size of the newborn is taken into account: the fieldmouse would otherwise stand no chance of competing with the elephant even though its kidneys might be far more efficient. For many years it seemed that this difficulty could be overcome by expressing results per unit of surface area; but when some workers gave their findings based on body-weight the limitations of both methods became evident. By either method the kidney of the human infant is immature in comparison with the fully developed organ; but, whereas on the basis of surface area certain of its functions, such as glomerular filtration, improve slowly and reach adult level about the second year, on the basis of body-weight the same functions at the same age pass through a peak well above adult standards.[3] The two bases of comparison cannot both be "right"; and we are forced to recognise that the only proper way of studying these processes is to establish their own framework of normality at different ages and to investigate them in their own right.[1 4]

Independently of arbitrary bases of comparison RENNICK and HAMILTON [5] have shown that isolated kidney slices from newborn animals do not pick up *p*-aminohippurate and tetra-ethyl-ammonium from the surrounding medium, nor do they concentrate these substances in the tubule cells, with the same mastery as preparations from adult kidneys; and evidence of similar immaturity as regards neonatal water, sodium-chloride, and ammonium-ion excretion [6–9] is now accumulating. Imbalance between certain glomerular and tubular functions has also been established in a wide variety of species; while least developed are those mechanisms which require not only a competent effector organ but also the integration of specific physiological detectors. Most newborn animals, for instance, will suck milk, but many will not take water by mouth in response to dehydration: only gradually do they learn how to register thirst and how to satisfy it.[10] And yet the volume and composition of their body fluids remain within relatively narrow limits, and the steady states proper to young animals are preserved. In the first few days of life their blood-urea rises; but the rise is small and its restoration to normal is rarely delayed beyond the first week.[11] It is becoming clear, moreover, that this readjustment does not reflect rapid maturation of the kidney (as has been thought in the past): urea-clearance takes much longer to reach a corresponding degree of efficiency. We are confronted here with a conflict between experience and experiment; and this conflict we must try to resolve.

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9. Cort, J. H., McCance, R. A. *ibid.* 1954, **124**, 358.
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Over a hundred years ago EDWARDS [12] recognised the overwhelming importance of growth in relation to many functions of the body: "dans la jeunesse", he wrote, "tout paraît tendre au développement et à l'accroîssement du corps". Since then, from time to time, other workers have pointed to the regulating influence of growth; but they lacked adequate experimental support and the implication of their remarks was missed.[1] In recent years, however, MCCANCE and WIDDOWSON [13] have found that nine-tenths of the protein nitrogen in the food of freely growing animals is incorporated directly or indirectly into tissue-proteins and is never presented to the kidneys for clearance as urea; and the same applies to a somewhat lesser degree to the more slowly growing human infants. Immature though their urea-clearance and *p*-aminohippuric-acid secretion is, they can maintain their blood-urea and blood-creatinine at normal levels provided that they are growing, and provided that they are not subjected to forced degradation of their tissue-proteins. On the other hand, in infants who have survived a protracted and difficult labour, and in newborn animals kept without food in a cold environment, the blood-urea rises steeply even though kidney function may be normal for their age.[14 15] A normal protein metabolism is not, however, the only stabilising effect of growth: a normal serum-potassium in piglets, a normal salt and water concentration in puppies, and a positive phosphate balance in babies have all been shown to depend on it.[16–20] The principle which emerges from these metabolic studies is that feeding in the neonatal period must aim at saturating as far as possible all growth requirements, without, however, overloading the baby's stabilising organs. In practice the problem is twofold: we must assess the growth-promoting value of various food, and we must balance this against the strain they impose on the infant's homœostasis. Much brilliant experimental and clinical work has shed light on the workings of enzyme systems at birth; and we can now explain such features as "physiological jaundice" in terms of enzymatic immaturity.[21–23] Like blood-urea, which reflects only one aspect of renal function, neonatal hyperbilirubinæmia is only one manifestation of enzyme insufficiency. Uridine compounds and their chain of enzymes—intimately concerned as they are with the conjugation and excretion of bilirubin—are involved also in the transport of aminoacids across the kidney tubules [24] and probably in the conversion of galactose to glucose in the liver.[25] Moreover, the work of DORMANDY et al.[26] suggests that immaturity of this conversion mechanism may not only deprive lactose of much of its growth-promoting value but also interfere with the utilisation and protective functions of glucose.[26]

Cessation of growth eventually leads to complete breakdown of internal stability, and this is incompatible with survival; but we are becoming increasingly aware that even minor setbacks (some of which may pass unnoticed at the time) may have disastrous consequences. Physical trauma has long been recognised as a cause of permanent defects and deformities. Biochemical trauma can be no less catastrophic—though most of its after-effects, especially damage to the central nervous system, we are only now beginning to discern. Much of it may be preventable—a prospect which makes this immensely difficult area of research the more challenging.

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27. The twelfth report of the Slough Industrial Health Service (1958–59) has lately been issued from the Central Clinic, Community Centre, Farnham Road, Slough, Bucks.

Annotations

MEDICAL ADVICE FOR INDUSTRY

A NEW pattern of industrial health service has been started at Newcastle. Following the lead of Slough,[27] cooperative services have hitherto been built round the swift and efficient care of industrial casualties and those taken ill at work. In creating the North of England Industrial Health Advisory Service, Prof. R. C. Browne has a more limited objective, which he approaches from his teaching and research unit and outpatient department at the Royal Victoria Infirmary. No casualty cover is being attempted, and the aim is rather to give advice on problems of two types. First, there will be medical advice for patients who have been away from work for more than a month. (These will be dealt with in conjunction with their own doctors, but will presumably be referred by managements.) Secondly, there will be an environmental service, covering investigations on the factory floor, library studies of relevant information, and laboratory work.

The membership subscriptions from firms will be 2*s*. per annum per employee—i.e., about a twentieth of the cost of a full casualty service. To sustain such a service at these rates may well require a coverage of between 50,000 and 100,000 workers, a formidable but not an impossible proposition. At the outset, a subsidy is essential, and this has come in the form of a grant of £11,500 from the Nuffield Provincial Hospitals Trust and £3000 from the King's College Students' Rag Trust. In addition, the staff of the Nuffield department of industrial health, two of whom are consultants in the National Health Service, are running the service in an honorary capacity. The cost of on-the-floor environmental studies will be substantial, and Slough experience has shown that an environmental hygiene laboratory eats up between £10,000 and £12,000 a year. For laboratory investigations the new service proposes to charge fees. The cover will ultimately extend to Northumberland, Cumberland, County Durham, and the North Riding of Yorkshire, being coterminous with the Newcastle hospital region. But at the outset the main emphasis will be in the indus-

trial area of Tyneside. The management of the service is in the hands of a small committee representing equally the University of Durham, industrial management, and the Trades Union Congress.

Clearly this is a pattern well worth trying. The value of the experiment lies largely in its application to a big area of existing industry. Progress will be judged by membership, by the volume of work done, and by the measure of financial success achieved. The headquarters of the service is 52, Leazes Terrace, Newcastle upon Tyne, 1.

At Slough [27] the work of the occupational hygiene department is no longer to be restricted to the neighbourhood but will become nation-wide. This development, towards which the Nuffield Provincial Hospitals Trust has given £3000, is described by Dr. Austin Eagger, the medical director, as the most ambitious experimental project on which the Slough Industrial Health Service has ventured. If it succeeds, the department will become an independent unit, associated with but not administered by the service.

INSTITUTIONALISATION

HOSPITAL treatment is not without its hazards for patients. The perils of staphylococcus, embolus, and slippery stairs must be faced in general hospitals, and the psychological evils of prolonged bed rest have been recognised.[28] The ill effects of lengthy residence in mental hospitals were described by Dr. D. V. Martin some five years ago,[29] and since then further evidence has accumulated. Dr. Russell Barton [30] has now gathered into a small space a great deal of information about institutional neurosis (as he calls it) as a disease entity in its own right.

The patient loses interest and initiative and tolerates unfair demands. His habits deteriorate. Passive submissiveness is punctuated by occasional outbursts of aggression on trivial provocation. The patient may be either apathetic or else active and cheerful, enjoying his simple life and taking part in handicrafts, but raising objections when discharge is suggested. The posture is characteristic, with hands held across the body, shoulders drooping, head sagging forward, and a restricted shuffling gait. The case-notes give clues to the onset of the neurosis with words such as " dull ", " solitary ", " childish ", and such ominous phrases as " has settled in well " or " gives no trouble ". It may not be easy to distinguish these symptoms from those of the later stages of the patient's underlying disorder (depression or myxœdema, for instance); indeed, the success of intensive rehabilitation may be the only guide.

As the cause of institutional neurosis, Dr. Barton points to the isolation from the outside world, which was deemed inevitable under the traditional mental-hospital regime, and to the enforced idleness of an orderly routine where nurses and maids do everything for the patients because it is " less trouble." " An arid vista of idleness " is his description of a day in a neat but dowdy long-stay ward. The authoritarian approach to the patient has much to answer for. Notices saying " Patients will not pick the flowers ", shouted orders, and the general belief that " they " are too mad to know what they want all foster the institutional state of mind. The rigid nursing hierarchy leaves the patient at the bottom of the " pecking order " to withstand the accumulated grievances handed down from above. Separation from personal possessions and old friends, the oppression of dull, noisy, or smelly surroundings, and the progressive loss of prospects in the world outside are their cumulative causes. Even drug therapy may tend to increase the patient's dependence on the hospital. Sedatives, Dr. Barton believes, are usually not only unnecessary but positively harmful; and he remarks wryly that more has been spent on advertising tranquillisers than on the whole of the Medical Research Council's work on mental illness.

Dr. Barton makes many useful suggestions for prophylaxis and treatment. He would like to see visitors allowed at any time during the day, though this might clash with his excellent 14-hour-a-day, 7-day-a-week, schedule of occupation. He is rightly concerned that occupation should be for the good of the patient and not only for that of the hospital. A useful worker, for instance, should not be left in the hospital sewing-room. The patient should be faced (though in a protected environment) with a real-life situation, for it is failure in such situations that has brought him to hospital. The term " institutional neurosis " may be disputed; for the state is seen elsewhere, particularly among solitary old folk deprived of social contacts by the passage of time or by personality traits. " Apathy reaction " might be better. Administrative psychiatry is coming into prominence again, and Dr. Barton has written a useful little textbook.

28. Asher, R. *Brit. med. J.* 1947, ii, 967.
29. Martin, D. V. *Lancet*, 1955, ii, 1188.
30. Institutional Neurosis. Bristol: John Wright. 1959. Pp. 56. 8*s.* 6*d.*

EDUCATION OF MONGOLS

" IT is of some administrative importance that there is a small but significant proportion of mongol children . . . with intelligence quotients within the range usually considered suitable for schools for the educationally subnormal." This is the key sentence in an article on another page of this issue by Dr. Dunsdon and her colleagues at the Clinical Genetics Unit (M.R.C.) at the Institute of Child Health in London. Mongols thought likely to be high grade were selected. Of a total of 390, 44 came for assessment; and in a further 8 cases estimates were supplied by medical officers of health. Taking an I.Q. of 45 as the minimum level at which a child has a reasonable chance of benefiting from education in a school for the educationally subnormal (E.S.N.), the report shows that 26 of the 390 came into this category, giving a figure for " educability " of 6–7%. The highest I.Q. in the series tested was 68, and there were 4 more with I.Q.s of 55 or over. At the time of selection 9 children were at a primary school, 23 were at an E.S.N. school, 15 were at private schools, and 7 were receiving home tuition. Most of the children at the E.S.N. schools and private schools of an E.S.N. type had kept their places by the time of the assessment, but as might be expected the primary-school placement had not proved successful.

Possibly something more than a minimal level of intelligence is necessary if a child is to be accepted as educable, and the present report approaches this on the basis of " social maturity " tests. From the small series available it seems likely that the response to education of the mongol with an I.Q. over 45 is more closely related to the " social quotient " than to the intelligence quotient alone. This should not, however, rule out the possibility of a trial within the educational system of the high-grade mongol. As Dr. Dunsdon and her colleagues point out, some still believe that no mongol is ever above the imbecile level. Most pædiatricians would confirm that from time to time they meet with a high-grade mongol for whom the possibility of admission to an E.S.N. school has not even been considered by the education authorities

until some pressure has been brought to bear. Probably this situation is improving, and the present report should help further. The degree, so to speak, of mongolism as shown by the classical features is no trustworthy guide to intelligence, and even the most "mongolian-looking" may surprisingly turn out to be not so low-grade as he looks. In the present report the objective triradius palm sign in the bright mongols is compared with the same sign in a control group, and no essential difference is recorded. The important point is that the possibility of education for mongols should always be considered even if for 94% this cannot in the end be achieved.

RENAL CHANGES IN ESSENTIAL HYPERTENSION

THE relation of renal arterial disease to essential hypertension is a subject on which much ink has been spilt. In the laboratory animal and occasionally in man narrowing of a main renal artery can undoubtedly produce an almost exact replica of essential hypertension. On the other hand it is very widely and firmly believed that high blood-pressure itself leads first to hypertrophy of the systemic arteries—that is, to an increase of plain muscle in the media and of elastic in the intima—and, later, to various degenerative processes (fibrosis, hyaline change, calcification) in both coats. This belief does not in itself exclude the possibility that structural disease of the renal arteries is the factor which causes essential hypertension. Such a possibility has often been suggested, but hitherto no-one has succeeded in demonstrating in early hypertension renal arterial lesions which cannot reasonably be dismissed as secondary to the hypertension—and the onus of proof clearly rests on the proposer. The latest challenger of the conservative view is Dr. William Evans.[1]

It must be recalled that Evans' definition of systemic hypertension is somewhat exacting; for he requires that the patient must show not only a persistently raised blood-pressure but also electrocardiographic evidence of left ventricular preponderance and radiographic signs of cardiovascular degeneration.[2] High blood-pressure alone, however severe, he regards as a labile physiological change which he terms hypertonia. Most workers do not subdivide hypertension in this way, and in the present state of knowledge it would seem to be a matter of opinion whether labile and fixed hypertension are separate entities or merely different aspects, stages, or intensities of a single disease. Indeed the dividing-line itself cannot be drawn with any assurance in the absence of continuous records of blood-pressure.

Evans advances the novel hypothesis that in essential hypertension the primary abnormality is a congenital deficiency of plain muscle in the media of lesser renal arteries. This hypoplasia, or even in places aplasia, of muscle is accompanied by fibroelastic proliferation of the intima which, by narrowing the lumen, causes renal ischæmia and consequent renal hypertension. He also describes fibrous narrowing or occlusion of arterioles, possibly secondary to thrombosis, and he suggests that what has hitherto been accepted as medial hypertrophy is in some vessels active contracture of medial muscle-fibres. One of Evans' main reasons for suggesting that the medial hypoplasia is congenital is that the incidence of polythelia (accessory nipples) is remarkably high in hypertension as distinct from hypertonia.[3] That heredity plays a part in essential hypertension is generally accepted; but it does not necessarily follow that the thinning of the media is congenital in origin. If the lesions are the cause of the hypertension they must involve the great majority of the lesser arteries of the kidney, because these vessels are end-arteries and patchy stenosis would cause focal atrophy or infarction and thence early and gross distortion of the surface of the kidney, whereas in early essential hypertension the kidneys usually appear either normal or finely granular. The histological evidence described by Evans comes from three groups of cases. The first was a group of normal controls. The second consisted of 13 patients who had died from complications of hypertension, and these are admitted to be advanced cases. The third group was composed of 3 patients, with evidence of delayed excretion of iodoxyl from one kidney, in whom unilateral nephrectomy caused only temporary remission of the hypertension. In each of these 3 cases (as well as in the 13 advanced cases) the excised kidney displayed the arterial lesions described by Evans. The ages of these patients were 63, 60, and 56, and in Evans' opinion these cases were examples of early hypertension caused by the lesions.

The prevailing and contrary view that arterial lesions of the kind reported by Evans result from the high blood-pressure is too well grounded to be easily reversed. Its supporters, aware that what most workers regard as benign hypertension may persist for years without causing symptoms, might reasonably argue that the observed thinning of the media is due to destruction or stretching of degenerate, atrophied, or even in some vessels necrotic muscle-fibres. And they might claim that evidence on such a vital and difficult question is admissible only when it is derived from patients—preferably young patients—who happen to die very early in the course of the disease and in whom the onset, not only of symptoms, but of the rise in blood-pressure can be accurately dated.

DIFFERENTIAL COOLING OF THE BRAIN

LOCALISED cooling of the brain may have certain advantages over generalised cooling of the whole body. The brain can thus be brought below the temperature at which the heart would fibrillate or stop (23–26°C). At such a low temperature (18°C [1]) the circulation to the brain can be completely cut off for up to 50 minutes in laboratory animals. The safe period for complete circulatory arrest under such conditions in man is not certain, but survival after periods of more than 14 minutes has been reported even with ordinary hypothermia.[2] If cooling is applied for the purpose of an operation with cerebral hypotension, the method need entail no more than carotid cannulation, a cooler, and a pump. The brain can be brought to 15–20°C while the rectal temperature remains above 29°C.[3] Cooling of the brain to less than 12°C is dangerous in itself, and produces neurological damage.

Woodhall et al.[4] have used a more completely isolated circulation to perfuse the brain by means of carotid and jugular cannulation. This necessitates the use of an oxygenator and the usual ancillary observations including flow, pressures, electroencephalography, and electrocardiography, as well as temperatures. They find that the brain can be rapidly cooled and rewarmed. Temperatures of 20°C are attained, at which level cortical

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2. Evans, W. *Lancet*, 1957, ii, 53.
3. Evans, W. *Brit. Heart J.* 1959, **21**, 130.

1. Kimoto, S., Sugie, S., Asano, K. *Surgery*, 1956, **39**, 592.
2. Lougheed, W. M., Sweet, W. H., White, J. C., Brewster, W. R. *J. Neurosurg*, 1955, **12**, 240.
3. Parkins, W. M., Jensen, J. M., Vars, H. M. *Ann. Surg.* 1954, **140**, 284.
4. Woodhall, B., Hall, K., Mahaley, S., Jackson, J. *ibid.* 1959, **150**, 640.

electroactivity ceases, and arteriovenous oxygen differences approach zero. There is a critical upper limit for perfusion-rates above which fatal cerebral œdema supervenes. The critical upper value is raised by hypothermia, but need not in practice be approached. With this method a leak from cerebral to general circulation of 12 to 45% has occurred in operations lasting 37–140 minutes. The leak is measured by adding 30 mC of ^{131}I to the closed perfusion circuit and sampling both that and the generally circulating blood at intervals.

The purpose of this isolated perfusion was to administer anti-tumour substances such as triethyl phosphoramide, ethionine, thienylanaline, and methionine sulphoxide in amounts that would have been fatal if applied to the rest of the body. Cooling was employed in an attempt to protect the brain, but unfortunately it also reduced the effect of chemicals on the cells of the neoplasm. Although the purpose of the experiment was thereby frustrated, the technical methods used remain of considerable interest, and can be applied in other directions. Thus the greater isolation of the circuit circumvents gross differential cooling of parts of the heart-muscle which, in the view of Lougheed and Kahn,[5] may lead to ventricular fibrillation even when the general body-temperature is only 35°C and that of the myocardium itself 32°C or over. The apparatus and supervision are, however, more complex and should not be employed if a simpler method is equally effective. Possibly gas bubbles rather than cold blood are the principal danger; and scrupulous prevention of bubbles, or the inclusion of bubble traps in the cooling circuit, may possibly prevent fibrillation at the higher temperatures of the myocardium. Both methods must still be considered by anyone contemplating differential cooling, and the choice would have to be determined by the purpose in view.

ADDICTION TO DRUGS

SERIOUS addiction to narcotic drugs is a small problem here compared with the U.S.A.: in New York City alone there are thought to be some 50,000 addicts, half of whom are under the age of 21 [6]; and 3 out of 4 women prisoners are said to be addicted.[7]

In the U.S.A. this great problem led to severe legislation in the 1920s and to the development of two special hospitals. The work of one of these, at Lexington, Kentucky (the other is at Fort Worth, Texas), was reviewed on Feb. 26 at the Maudsley Hospital, London, by Dr. Harris Isbell, director of the research programme.

Called the U.S. Public Health Service Hospital, it was started in 1935, and houses about 1100 addicts, of whom 75% are long-term detainees from the courts and the remainder short-stay voluntary cases. Negroes and Puerto Ricans are much overrepresented, and the peak age is 20-30.

The patients mostly have a disorder of character, with superadded depressive, schizoid, or neurotic traits. Treatment is by graded withdrawal of drugs, physical rehabilitation, and occupational regimes, with group therapy for some. Because of long distances social work is the weakest part of the programme; and the relapse-rate is high, about 40% of patients requiring readmission.

A main goal of the research programme has been the discovery of an effective analgesic free of addictive properties. So far nalorphine has come nearest the mark, but the risk of toxic psychosis precludes wide usage. Dr. Isbell believes that juggling further with morphine molecules will not help, and success, he emphasised, would not materially alter the overall prevalence of addiction; nor, he added, would extension of the heroin ban to these or any other islands.

Clinical observations have led Dr. Isbell and his colleagues to elucidate two main physiological patterns of addiction. Withdrawal of opiates after long and heavy dosage causes much distress with increased irritability of the central nervous system, but of a type different to that after withdrawal of barbiturates, alcohol, and meprobamate (and probably paraldehyde and chloral), where convulsions and delirium occur and the patient is in greater danger. Neurophysiological studies on dogs by Dr. Abraham Wikler have shown that the addiction to opiates involves the central nervous system at all levels in a diffuse manner and that withdrawal symptoms (which are truly physiological and independent of personality factors) accompany hyperirritability in neurone circuits. The personality, however, determines the emotional reaction to the withdrawal illness. The other important drugs —marihuana and cocaine—seem to act differently; for, while physiological dependence and withdrawal symptoms are not found, psychotic complications may make addicts a danger to themselves and others. Dr. Wikler is engaged in testing his hypothesis of specificity in drug action: opiates, he believes, depress the primary drives and are taken because of anxiety about these drives; while alcohol and barbiturates are taken by those who need to feel aggressive and masculine.

Prof. Isidor Chein,[8] who has studied the social aspects of 'teenage drug-taking in New York City, suggests that crime among addicts is an effect of the illegality of drug-taking. But addicts, he says, are abnormal people. They usually come from underprivileged groups with disrupted family life and are likely to show a " delinquency orientation " comprising rebellion against authority, rejection of middle-class standards, a sense of pessimism and of " being an outsider ", and a high value placed on power over others, thrills, and taking chances. (Amphetamine addiction in Japan has also been shown to correlate with juvenile delinquency.[9])

" Addicts ", says Professor Chein, " are individuals who are not able to enter prolonged, intimate relationships with either peers or adults; they are frequently overcome with a sense of futility, expectation of failure, and general depression; they are easily frustrated and made anxious, psychological states under which they find it harder than most to stand up; and the males manifest a variety of difficulties in assuming the masculine role."

From these personality characteristics, a prediction was made as to the type of early home backgrounds likely to produce them; and, on exploration, such conditions were found in every case. Professor Chein concluded:

" Personality trends produced by these early home environments of the addicts-to-be are reinforced by the experiences of the larger environments they encounter when they begin to leave the dubious shelter of the home. It is a story of enforced depression of the human spirit. It is not even a story of contagion. It is a story of despair."

Contagion, however, should not be neglected, for without the drugs there could be no addiction.

5. Lougheed, W. M., Kahn, D. S. *J. Neurosurg.* 1955, **12**, 226.
6. *News Chronicle*, Feb. 3, 1960.
7. *Times*, Feb. 29, 1960.
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Special Articles

PSYCHIATRIC HALFWAY HOSTEL

A Cambridge Experiment

D. H. CLARK
M.A. Cantab., M.B. Edin., F.R.C.P.E., D.P.M.
HONORARY CONSULTING PSYCHIATRIST

L. W. COOPER
WARDEN

WINSTON HOUSE, CAMBRIDGE

IN recent years there has been great interest in the rehabilitation of the mentally sick, especially those who have spent many years in mental hospitals. Day hospitals, night hospitals, hospital industries, industrial rehabilitation units have all contributed to this work, and "halfway houses", or sheltered residential accommodation, have often been suggested as another possible means of helping these people to rejoin the community.

In 1956 the Cambridgeshire Mental Welfare Association, a voluntary organisation founded in 1905, approached the Cambridgeshire County Council with a proposal to set up a halfway house in Cambridge; the project was accepted in principle but no funds were available. In 1958 the S.O.S. Society, a national philanthropic body specialising in the provision of hostel accommodation for the socially unfortunate and handicapped, offered a house in Cambridge, and Winston House was opened in October, 1958. The society have financed the experiment (with aid from the Association and the county council) and a local committee has guided the day-to-day management.

THE RESIDENTS

Winston House has places for 12 men and 11 women and when it was opened it was expected that there would be considerable competition for places. At no time during the first year, however, has the house been full and the average number of residents has been 16.

Selection

Residents are selected by a small committee. The original criteria of selection stated:

"The age range of residents would be from twenty-five to sixty-five years, but it is expected that few over the age of fifty will be accepted; mental defectives will not be accepted, unless capable of social rehabilitation. All applicants should be in employment, or capable of obtaining it almost immediately."

In fact, of the 36 residents, 5 were under twenty-five, 2 were mental defectives (though they were both in employment when they entered the hostel), and several residents were admitted when not in employment. The criteria have broadened and at present can be fairly stated as follows:

Residents should have had a mental or nervous illness and be in work or capable of finding employment within a month. They should be capable of rehabilitation—i.e., there should be a good chance of their achieving reasonably independent social life (in lodgings at least) within six months.

In the first year there have been 41 admissions and 22 discharges, but as there were some readmissions the total number of people considered in this study is 36 (23 men and 13 women).

Background

26 came direct from Fulbourn Hospital, 3 came from the Cambridgeshire Mental Welfare Association, 2 from the Addenbrooke's Hospital psychiatric outpatient department, 2 from a general practitioner in Cambridge, 1 on his own initiative, and 2 by arrangement from other hospitals. All but 3 had been for a long time in an institution, nearly all in mental hospitals. All the patients were completely discharged from their hospitals before they came to Winston House.

Some were on chlorpromazine or other tranquillisers; often it was possible to cut this down, but some have had maintenance doses for months. Some receive regular sedation.

The average length of previous hospital treatment was four years, nine months. 1 resident had been continuously in Fulbourn Hospital for nineteen years. 6 residents had been in hospital for more than ten years and altogether 16 residents had more than two years' continuous residence in an institution.

19 had suffered from schizophrenia; 5 from depression; 2 from manic-depressive psychosis; 2 from epilepsy; 2 from mental defect with emotional instability, and 6 from other disabilities—e.g., psychoneurosis, personality disorder, alcoholism.

15 men and 11 women were single; 2 were divorced, 3 separated, and 3 widowed. Only 2 of the 36 had a spouse still interested in them.

The average age on admission was thirty-seven years. 3 residents were fifty-six and 1 was nineteen. 5 were over fifty; 9 between forty and fifty; 13 between thirty and forty; and 9 under thirty.

The average resident was thus an unattached man or woman in the middle thirties with a long history of mental hospital treatment. Most of them had been working outside hospital, but had failed to re-establish themselves in the community. When they first came to Winston House they were docile, passive, and obedient; they worked all day and came back and sat watching the television at night. As time went on, and they came to realise that they were free from the hospital organisation, they began to go out to the pictures and the pubs, to buy clothes and bicycles, and show signs of social initiative. After some months they would find lodgings or move off.

Length of Stay

No residents left immediately after arrival, though 4 who were accepted did not come in.

3 residents stayed for four weeks or less, but all 3 were satisfactory discharges who had benefited from their stay. The average period of residence was twenty-two weeks; the shortest stay was two weeks, and the longest stay was forty-five weeks.

Discharges

During the year there were 22 discharges.

4 residents had to go back to hospital. 1 alcoholic started to drink intermittently soon after his arrival. He remained in work for some weeks but the struggle steadily became more difficult for him until it was clear that the best thing for him was to return to the hospital. The 2 men with manic-depressive psychosis had to return to hospital. Both had a long history of remissions and relapses into hypomania. The fourth return to hospital was a forty-eight-year-old man with paranoid schizophrenia. The other 18 discharges were reasonably satisfactory. 2 patients went to their relatives; 6 went to lodgings which had been arranged for them with our approval, and 10 made their own arrangements, 1 slipping away without giving warning.

THE YEAR'S RESULTS

Of the 36 people admitted during the year 17 were still in Winston House; 19 had gone elsewhere. The older residents had done less well than the younger. Of the 5 men over fifty, only 1 had been discharged; of the 9 residents under thirty, 7 had been discharged. When analysed by diagnosis some striking trends emerged.

Of the 19 residents with schizophrenic illnesses, 9 were still in Winston House (though 5 had been there less than three months), but 10 had been discharged satisfactorily. Of the 5 residents with depressive illnesses only 1 had been discharged, and 4 remained in Winston House (though 2 had been admitted within the past three months). The 2 men with manic-depressive psychosis had both returned to hospital, but 1 had come back to Winston House. 2 residents with epilepsy had both left and were in the community, though still having difficulties. The 2 mental defectives with behaviour disorders had also left and had not been readmitted to an institution though their balance was known to be rather precarious. Of the 6 patients with psychoneurosis and personality disorders, 3 were still in the house and the other 3 had left, though only 1 had an entirely satisfactory discharge.

A follow-up of the 19 discharges suggested that of the 13 residents who had been away from Winston House for more than a month 6 would not have achieved this degree of independence but for their stay.

1 had died; he made a satisfactory rehabilitation and slipped away from Winston House but he died two months later of heart failure in a lodging house in London. 2 were in Fulbourn Hospital. 7 were satisfactorily settled, 2 with relatives and 5 in lodgings in Cambridge. 9 were managing fairly well; 3 of these had only been out of Winston House a few weeks but the other 6 were maintaining a reasonable balance either in their homes or in their lodgings.

LIFE AT THE HOSTEL

The hostel is a large Victorian house in what was a residential road. The residents are in dormitories, 1 two-bed, 2 three-bed, 2 four-bed and 1 seven-bed; there is a common room and a dining-room. There is a staff of 4.

The warden has tried to run the house as a place in which the residents could adjust their way of life to a more normal pattern and could learn to appreciate that they are discharged from hospital and living in communal lodgings.

A " code of behaviour " rather than a " set of rules and regulations " has been set up and an effort has been made to create an atmosphere of homeliness and relaxation. Attendance at Sunday morning family prayers has grown from 1 or 2 to 13 or 14. A reading and quiet room has been opened and a therapeutic social club was started in September, but has not so far attracted many residents. Attempts have been made to get the residents to help in running the hostel but meetings have been poorly attended. The staff join the residents for meals which are taken at separate small tables.

The very close connection of residents with each other and Fulbourn Hospital has tended to give the impression that residence in Winston House is an extension of their hospitalisation; and conversation centres around hospital life. All the staff have been asked to treat residents as normal people and to make no reference to the past. The atmosphere in the house has been reasonably good except for the first month or two. The first intake of residents included one or two who were unsuitable and who, by their difficult behaviour, caused some unrest and discontent. A few admissions from hospitals outside Cambridge have brought a new outlook.

The staff found at first a background of mistrust, suspicion and indifference among the residents, but by the end of the first year there seemed to be more trust and confidence in the staff and the hostel as a way back to normal life.

The year's experience suggests that single rooms for all residents would be an advantage. There have been complaints of nocturnal strolling, heavy asthmatical breathing and coughing, eczema scratching, fear of the dark with a consequent desire for night lights, and early bathers.

SOME FIGURES

During the first twelve months the running costs (food, light, heat, staff salaries) were £4514. The average weekly cost per resident (including all meals at weekends) was £6 13*s*. 7*d*. The residents actually paid £3 15*s*. per week (for a few reductions were allowed). The loss on the year was £1784.

The deficit is partly due to the fact that the house was building up numbers during the first five months and even later was never full. On the assumption of an overall average of 21 residents the weekly cost per resident per week would be £4 2*s*. 8*d*.

These costs make no allowance for the capital cost of the house, for its repairs, or for the administrative service of the S.O.S. Society's central office staff.

DISCUSSION

It is difficult to answer the question: " What did these people get from their stay in Winston House? ", for this varied for different people. Many long-stay hospital patients said that it was a great pleasure to live again in a home. They enjoyed the privacy of the small rooms and the freedom to come and go. For others, the security of the house was important, and during their stay they were able to make progress in their psychotherapeutic treatment or personal development. Some of course resented the regime, but the tolerance with which criticism was accepted and the way in which it was met by pointing out the needs of the other residents was at times therapeutic and educative. The people who gained most were undoubtedly the long-stay schizophrenics who had no home or interested relatives. Without Winston House they would have stayed forever in mental hospitals. With it some of them managed to achieve an independent life.

The work has been exacting and at times perplexing. Residents have become disturbed in a psychotic manner and have even wandered round hallucinated in the middle of the night. The lack of response from the residents and their disinclination to form any group or relationships with one another has been striking. A clinic has been held in the house every week at which residents were seen, especially for adjustments of medication. Though no formal psychotherapy has been carried out at these evening clinics, they have had considerable supportive value. The consultant psychiatrist, or a deputy, has always been available for consultation. In future it is hoped to hold these clinics at a nearby hospital outpatient clinic.

Some of the original expectations with which the house was set up have not been justified. It was known that there were enough patients working out from Fulbourn Hospital to fill such a half-way hostel, but the criterion that they should be capable of rehabilitation proved limiting. In the months before the opening of Winston House there was an average of 25 patients going out to work from Fulbourn Hospital every day. Some of these were moved to Winston House during the autumn of 1958 and the number of working patients fell, but there have never been less than 10 patients going out to work every day from Fulbourn, and during the summer of 1959 the average was about 15, yet none of these was judged suitable for the vacancies at Winston House. Some were short-stay patients, working outside the hospital before returning to their homes. Others were long-stay patients for whom there was no prospect of rehabilitation.

The preliminary phase of build-up ended during February, 1959, and since then there has been an average of 16 residents or more. A mental hospital serving a catchment area of 360,000 population will probably only have about 16 patients at any one time suitable for and in need of a halfway hostel. Since August, 1958, we have tried to interest other hospitals in the venture, but so far the number of applicants has been small. This may be because even though recovering patients have no homes, they have roots in their native community and, however keen they may be to leave hospital for a halfway house, they hesitate to go to a distant city and an unknown part of the country.

CONCLUSIONS

A halfway house for psychiatric patients capable of paid employment is of value for a limited group of people. The patient who gains most seems to be the schizophrenic between 30 and 45 whose illness has passed the acute stage, who has lived for a number of years in a mental hospital, and who is capable of regular work in the community but not able to achieve an independent social life, either because he lacks interested relatives or initiative.

COMMITTEE ON ACCIDENT SERVICES

IN a memorandum published a few months ago [1] the British Orthopædic Association set out the present deficiencies of hospital accident services in this country and made a number of recommendations. A further step towards improving this part of the work of the National Health Service was announced this week. On the initiative of Mr. H. J. Seddon a conference on accident services was held in January at the Royal College of Surgeons of England; and it set up a committee which is to examine the situation and make proposals. The chairman of the new committee is Mr. H. Osmond-Clarke, and the sponsoring bodies are the Royal College of Surgeons of England, Edinburgh, and Ireland, the Royal College of Physicians of London, the College of General Practitioners, the British Medical Association, the British Orthopædic Association, the Society of British Neurological Surgeons, the Society of Thoracic Surgeons of Great Britain and Ireland, and the British Association of Plastic Surgeons. The committee's recommendations are in due course to be passed to the Joint Consultants Committee for discussion with the Ministry of Health.

MEDICAL LIBRARY FOR AUCKLAND

FROM OUR NEW ZEALAND CORRESPONDENT

Sir Ernest Davis, of Auckland, has given £36,000 to build and partly maintain a medical library and meeting-rooms for professional purposes in the precincts of the Auckland Hospital. This will replace the central medical library at present housed and almost wholly maintained by the Auckland Hospital Board, the nucleus having been formed many years ago by the late Dr. T. M. Philson, a former medical superintendent.

Sir Ernest's gift is particularly welcome at the present time. Medical research has begun in Auckland in the last few years, and at some time in the future a medical school will be developed. The Committee on Universities, under the chairmanship of Sir David Hughes Parry, lately suggested that the plan for the second medical school and the proposed veterinary school should be shelved for ten years in view of the enormous arrears to be made up in buildings, staffing conditions, &c., in the university institutions. But persistent difficulties in staffing the hospitals at the more junior levels, and other factors, may bring about a more urgent view.

1. Summarised in *The Lancet*, 1959, ii, 78.

Occasional Survey

FLUORIDATION: THE PRESENT POSITION

THE new year began with a reawakening of the controversy over the fluoridation of water-supplies. Dr. Norman Parfit, medical officer of health for Abingdon, says in his annual report that any further delay in fluoridation is "quite inexcusable" [1]; and he adds that although the next two years should bring more positive evidence (the fluoridation tests in Watford, Anglesey, and Kilmarnock end in 1961) "previous investigations have amply demonstrated the good effects of fluoridation." Dr. Wynne Griffith, county medical officer for Anglesey, has also advocated the general adoption of fluoridation, saying that "decay advances so fast that the child is already a dental cripple when the school dental surgeon first sees him",[2] and that "fluoridation costs about 6*d*. a head of the population for about a year. A very small price to pay for reducing the amount of decay by a third." [3] Now we read that the States of Jersey have rejected by a large majority a bill for the compulsory fluoridation of water-supplies.[4] These pronouncements coincide with the appearance of a critical analysis by Sutton [5] of the results of five of the recent fluoridation trials in Canada and North America. His discussion relates mainly to the statistical conduct of the trials, but a brief recapitulation of the story of the connection between fluorides, enamel dysplasias, and resistance to caries is necessary to provide the background against which his work must be judged.

As long ago as 1874, a Dr. Erhardt, of Emmerdingen, described an experiment in which a dog's molar tooth was extracted, after which the dog was given small doses of potassium fluoride for four months. The opposite molar was then removed and was found to be harder and denser. Dr. Erhardt recommended the sucking of one fluoride pastille a day for the protection of the teeth against caries; according to him such a practice had been known in England for several years, but no reference can be found in contemporary medical literature before 1892.[6] In that year Sir James Crichton-Browne stated that a supply of fluoride was necessary when teeth were developing.[7]

The effects of excessive fluoride intake on dental enamel were first noticed nearly sixty years ago among the inhabitants of Naples, and, at about the same time but independently, by dentists in Colorado Springs. In 1908, the Colorado Springs Dental Society began a study of the "Colorado brown stain". Much of the initial work was carried out by Black and McKay, whose first report was published in 1916.[8] They did not comment on any reduction in caries incidence, for their concern was with the pathology of mottled enamel. After Black's death, his work was continued by McKay, who reported in 1929 that children with mottled enamel were less susceptible to caries than those with normal teeth.[9] A similar observation had been made by Bunting in 1928 [10] The connection with fluorine was not appreciated, however, until 1931 when Churchill analysed the water of certain districts where mottled enamel was

1. *Sunday Times*, Jan. 10, 1960.
2. *Liverpool Daily Post*, Jan. 28, 1960.
3. *Sunday Times*, Jan. 17, 1960.
4. *Times*, Feb. 10, 1960.
5. Fluoridation: Errors and Omissions in Experimental Trials. By PHILIP R. N. SUTTON, D.D.SC. London: Cambridge University Press. Melbourne: Melbourne University Press. 1959. Pp. 83. 8*s*. 6*d*.
6. Banus, J. *Penguin Science News*, 1955, **38**, 27.
7. Crichton-Browne, J. *Lancet*, 1892, ii, 6.
8. Black, G. V., McKay, F. S. *Dental Cosmos*, 1916, **58**, 129, 477, 627, 781, 894.
9. McKay, F. S. *ibid*. 1929, **71**, 747.
10. Bunting, R. *ibid*. 1928, **70**, 1002.

endemic, and found that fluorides were present in concentrations between 2 and 13·7 parts per million (p.p.m.).[11]

At about the same time, Smith and her coworkers at the University of Arizona were conducting animal experiments from which they discovered that fluorine in the diet could produce the typical lesions of mottled enamel.[12 13]

The action of fluorine on the tooth is still uncertain—it may be a surface effect, or it may be a systemic one, the fluorine entering the tooth during the formative period. A less likely hypothesis is that there is an inhibition on the tooth surface of bacterial and enzymatic processes. There are, however, some facts that are well established. Fluoride ions can replace hydroxide ions isomorphously and reversibly, and this can occur in both bones and teeth. The extent of this replacement in living teeth depends upon the amount of fluorine ingested.[6] "Normal" enamel contains about 0·02% of fluorine and "normal" dentine about 0·025%; mottled teeth in Maldon contained about 0·032% and 0·073% respectively. Pure calcium hydroxyapatite contains 4% of fluorine, but this figure is never approached in enamel, and so long as the enamel remains permeable, replacement can continue—at least, in theory. Finally, calcium fluorapatite and calcium fluoride are less soluble in water than either calcium hydroxyapatite or calcium carbonate.

A point that has been raised in the *Sunday Times*[14] is that the optimum fluoride level of 1·2 p.p.m. for caries control actually lies within the range that will produce dental fluorosis. Now the generally accepted fluoridation hypothesis is that "a concentration of about 1 p.p.m. of fluoride in the drinking water, mechanically added, inhibits the development of dental caries in the teeth of the users of the water,"[15] and, so far as is practicable, most fluoridation projects aim at maintaining concentrations of 0·9 to 1·0 p.p.m. A concentration of 1 p.p.m. can cause very mild mottling in about 10% of those exposed, but the mottling can be detected by expert examination only.[16] The fluorosis produced at levels between 1·5 and 2·0 p.p.m. is still mild, and, although not desirable, is inconspicuous. Fluoride levels in the neighbourhood of 6 p.p.m. are usually necessary before the mottling becomes severe and disfiguring. It must be remembered that the pigmentation which then appears is not caused by the fluoride ion, but by the absorption of strongly coloured ions, such as those of iron and manganese.[13] Furthermore, there is a possibility which has not yet been fully looked into that other members of the halogen family of elements may, in fairly large doses, produce mottling.

Further evidence tending to prove the harmlessness of fluoridation at the proposed level is provided by Chalmers Clarke and Mann,[17] who examined the teeth of children in the Deeping St. James schools, in South Kesteven, Lincolnshire. The public water-supply in this area is naturally fluoridated to 2·5 p.p.m., and in well-water the concentration reaches 4 p.p.m. They found that the mottling of the enamel in children who drank water from the public supply was very mild and unlikely to be detected by any but experienced examiners. The well-water produced obvious mottling, and the white patches became discoloured as the children grew older; with levels below 4 p.p.m. this colour change did not occur. The report includes an interesting and valuable account of the hydrogeology of a natural fluoride area. The only criticism that can be made is that the number of children examined was small (56) and the method of selection was not given; although it was stated to be "random", it is not clear whether this word was used in its strict statistical sense.

Most of the pioneer investigations in the United States were made by Trendley Dean, senior dental surgeon of the United States Public Health Service, and reference to his published work may be found in the report of the United Kingdom Mission on Fluoridation.[18] The first observations in this country seem to be those of Ainsworth[19 20] in Maldon, Essex, where the natural water supply contains 5 p.p.m. of fluoride. These were followed by the reports of Weaver[21] on the dental condition of the children in North and South Shields.

The state of Wisconsin has led in the fluoridation of water-supplies as a public-health measure,[16] but the water department of New York has always opposed fluoridation for a number of reasons, which have been set out by Nesin,[22] and, after a public hearing in March, 1957, the proposal was finally shelved. Nevertheless, by 1954, it was estimated that approximately 40% of the population of the United States receiving public water-supplies were getting fluoride at a concentration of at least 0·9 p.p.m.[23]

Much of the recent evidence in favour of fluoridation has come from the trials in Brantford, Canada, and in Grand Rapids, Newburgh, and Evanston in the United States. Not everyone would agree with Sutton,[5] however, that these trials provided the main experimental basis that led to the inauguration of many fluoridation programmes; the work of Trendley Dean, Ainsworth, and Weaver cannot be lightly discounted. All the same, Sutton has been able to show that the American trials claim more and prove less than the published results at first suggest. Some of his contentions demand careful attention from the planners of fluoridation experiments that they may be aware of the pitfalls which could (and often should) have been avoided.

Obviously any study of the effects of fluoridation must have adequate controls; of the five trials dealt with by Sutton, one (Branston) made no use of controls, while the other four had controls which were by no means ideal. The choice of a control city or community is not so easy as it may seem: in all respects it must resemble as closely as practicable the area in which fluoridation is to be carried out. Fisher has said that "the uncontrolled causes which may influence are always strictly innumerable,"[24] but there are certain factors which do not seem to have received the recognition they deserve. The water-supplies of the two areas should be as nearly the same as possible; the degree of hardness of the water may well affect the absorption of the fluoride ion, as may the presence of trace quantities of other ions. In none of the trials were detailed analyses made of the water-supplies. Climate can also influence the amount of water, and hence the amount of fluorine, ingested, so the climates of the two areas should resemble one another closely. A third criterion is that the caries-attack rates in the areas should be closely comparable in the age-groups considered. This can be determined only by conducting at least one survey

11. Churchill, H. V. *Industr. Engg Chem.* 1931, **9**, 105.
12. Smith, M. C., Smith, H. V. *Univ. Arizona, Coll. Agr. exp. Stat. tech. Bull.* July 15, 1932, no. 43.
13. Smith, M. C., Lantz, E. M. *ibid.* Jan. 1, 1933, no. 45.
14. *Sunday Times*, Feb. 7, 1960.
15. Brown, H. K., McLaren, H. R., Stewart, B. J. *J. Canad. dent. Ass.* 1954, **20**, 585.
16. United Kingdom Mission Report. The Fluoridation of Domestic Water Supplies in North America; p. 2. London, 1953.
17. Chalmers Clarke, J. H., Mann, J. E. *Brit. dent. J.* 1960, **108**, 181.
18. *ibid.* p. 99.
19. Ainsworth, N. J. *Roy. dent. Hosp. Mag.* 1928 **2**, 2.
20. Ainsworth, N. J. *Brit. dent. J.* 1933, **55**, 233.
21. Weaver, R. *ibid.* 1944, **76**, 29; *ibid.* 1944, **77**, 185.
22. Nesin, B. C. *J. Maine Water Util. Ass.* 1956, **32**, 33.
23. Fluoridation as a Public Health Measure. Symposium Volume of the American Association for the Advancement of Science. Washington, 1954.
24. Fisher, R. A. The Design of Experiments; p. 2. Edinburgh, 1951.

in each of the areas that may otherwise appear suitable. Strictly speaking, which area is to receive fluoridated water and which area is to act as a control should be determined by some random procedure. This is, perhaps, a counsel of perfection and is not nearly so vital as an assessment of the variability of the caries-attack rate. In the Grand Rapids study, Arnold [25] mentioned this variability, but its importance was either not fully realised or was ignored, just as it was in the other trials. Sutton emphasises that the method generally used for calculating the change in the decayed-missing-filled rate (D.M.F. rate) of the permanent teeth (original D.M.F. rate minus the most recent D.M.F. rate, expressed as a percentage of the original rate) is particularly sensitive to small variations in the original rate. This also applies to the other statistic—the decayed-extracted-filled rate—used for the deciduous dentition.

In none of these trials was an attempt made to determine either the "between-examiner" or the "within-examiner" variability; that such a variation must exist was recognised in some of the trials [26] but the methods adopted to minimise it were, to a statistician, somewhat peculiar. The situation was further complicated by the use of bite-wing radiography in some examinations and not in others.

The difficulties of obtaining a random and unbiassed sample from a given population are well known, and some degree of selection had to be adopted in the American trials. For example, in the Evanston study, Negroes were excluded as their caries-attack rate was considered to differ significantly from that of the white children. A similar selection was made in New Zealand when Maori children were excluded from a recent fluoridation survey.[27] Clearly, the less selection that has to be exercised in taking a sample, the better.

A small point that can be criticised both in the published results of the trials and in Sutton's analysis of them is that there is a tendency to quote some findings to more significant figures than would seem to be justified. D.M.F. rates given to two decimal places have an appearance of authoritativeness that may be unfounded, and investigators should remember Huff's comment: "For a spurious air of precision that will lend all kinds of weight to the most disreputable statistic, consider the decimal." [28]

Sutton's conclusion is that the trials he discusses do not provide a sound basis for the establishment of fluoridation; but, to keep matters in perspective, it must not be forgotten that there have been earlier and later trials of equal significance. Sutton's work will undoubtedly have a mixed reception: those who are opposed to fluoridation will be provided with plenty of ammunition, but the others should not be dismayed and should decide to look more closely at the design of their experiments so that their results may be as unassailable as possible. A generally acceptable schedule should be drawn up stating precisely what figures are wanted to avoid the frustration of finding that valuable information has been lost by indiscriminate grouping of some sets of figures, and by the complete lack of others. Sutton's investigations should be regarded not so much as an attack on fluoridation itself as a criticism of some lax and unconventional statistical procedures.

25. Arnold, F. A., Jr., Dean, H. T., Knutson, J. W. *Pub. Hlth Rep., Wash.* 1953, **71**, 652.
26. Ast, D. B., Bushel, A., Wachs, B., Chase, H. C. *J. Amer. dent. Ass.* 1955, **50**, 680.
27. *Lancet*, 1959, i, 563.
28. Huff, D. How to Lie with Statistics; p. 106. London, 1954.

After studying even a small part of the mass of data in the literature of fluoridation, one is tempted to agree with the anonymous writer who said, "the fact that these results are not statistically significant only confirms our view that it is clinical judgment that counts, and in no way invalidates our findings." [29]

29. *Lancet*, Feb. 6, 1960, p. 332.

Medicine and the Law

Psychiatric Treatment in Prison

A MAN aged 30, with a history of pathological shyness and mental ill-health, wished to marry. He advertised in a newspaper and so met a nursing sister to whom he became engaged.

At the time he was living away from his parents' home. The relationship became unhappy and his fiancée eventually told him that she had finally finished with him. The man felt that his one chance of happiness lay in marrying her. He bought a knife and some strychnine tablets and visited her home, intending to kill both her and himself. He went to her bedroom, where she lay asleep, and struck at her head with the knife. At the very moment of striking the blow he suffered a change of heart and held back, with the result that a flesh wound only was inflicted. He waited with the girl while police and medical help were summoned.

He was charged with wounding with intent to murder and wounding with intent to cause grievous bodily harm. While awaiting trial he was released on bail and went to live at his parents' home, receiving five weeks' inpatient and, later, outpatient treatment at a nearby hospital, which greatly improved his mental condition. At the trial he was acquitted of the first charge but convicted of wounding with intent to commit grievous bodily harm. Medical evidence called on his behalf was that further violence was unlikely, and that his mental welfare would be best served by outpatient treatment. The trial judge observed, however, that the paramount consideration must be the interest of the public, and sentenced him to three years' imprisonment.[1] He appealed against his sentence.

It was said on his behalf that the day after the sentence he attempted suicide. He recovered and remained in prison where, despite the provisions of the Mental Health Act, 1959, he received no psychiatric treatment.

The Lord Chief Justice observed that that was not the fault of the authorities; such treatment would not be given to a prisoner while an appeal was pending.

Counsel said that a fortnight before the appeal the man was removed to another prison where he was kept in a ward with ten other prisoners, all of them psychological cases. The man was fast sinking into schizophrenia.

A doctor in charge of the man's treatment while he was an outpatient gave evidence, and said that he had found him changed for the worse just before the hearing of the appeal: he was more tense, shy, and despondent. The conversation in the ward with the other prisoners, of whom four were homosexuals, was almost perpetually on the subject of homosexuality. Already the man was suffering intensely, and if he were kept in prison for another 18 months the witness would not guarantee that he would be fit to be at large. The medical officer of the prison, called by the Crown, said that the men in the ward were undergoing group-analysis and the homosexual elements, present in everyone's character, became unveiled. There was no serious danger of the defendant's being driven to a homosexual relationship and the interaction of personalities was very beneficial. The witness was not surprised that the man found his treatment intensely disagreeable. The witness admitted that he had no specialist qualifications in psychiatry.

The LORD CHIEF JUSTICE, giving judgment, said that by reason of the fresh medical evidence which had been called the court had come to the conclusion that the man should be released on probation, with a condition under section 4 of the Criminal Justice Act 1948, that he should reside at a mental hospital for 12 months from the date of the conviction, the greatest length of time which could be ordered. The order was made on the basis that the man himself was anxious to continue his treatment for as long as necessary and the court looked to the man's parents to arrange for whatever further treatment was necessary.

Regina *v.* Cleverley.—*Court of Criminal Appeal:* Lord Parker, *C. J.*, Cassels and Ashworth, *JJ.* Jan. 14 and Feb. 1, 1960. Elwyn Jones, Q.C., and Julian Priest (Cava & Lougher, Cardiff); Tasker Watkins (Director of Public Prosecutions).

GROVE HULL
Barrister-at-Law.

The Patient—not the Textbook

On May 25, 1954, a school doctor saw a fifteen-year-old boy in the sick-bay. The boy told the doctor that he felt perfectly well, but the doctor came to the conclusion that he had a mild attack of infective hepatitis.

He put the boy on a full fat-free diet and glucose, and told the sister to keep him in bed. The boy's condition improved and on May 29 the doctor allowed him to get up in his room and on June 1 to go out round the school grounds. The doctor visited the boy daily and the improvement continued. The symptoms had not completely disappeared by June 5, but the boy had a general feeling of well-being and his improvement was such that the doctor allowed him to go home for the mid-term weekend; the doctor was influenced by the facts that the boy had a mild form of epilepsy and would have been heart-broken if not allowed to go home, and that an emotional disturbance might have had some effect on his epileptic condition. The boy returned from his weekend on June 8, and on the following day he had a relapse. Later he was taken to hospital, but despite every possible treatment his condition deteriorated, and in 1957 he died from cirrhosis of the liver.

The boy's father sued the school and the doctor alleging negligence, in that, in effect, the doctor had treated the case too lightly, had allowed the boy out of bed too soon, had run unjustifiable risks, and had departed from the orthodox treatment for the disease.

It was said that a general practitioner should be guided by the standards of learning existing at the particular time, which standards he should adopt for the purposes of ordinary treatment, and various textbooks and articles were referred to as showing that to avoid a relapse the orthodox treatment was to keep a patient in bed at complete rest for a definite period after the symptoms of the disease had cleared up. Expert medical evidence was also given on both sides. It was conceded that the school would not be liable in negligence unless it was vicariously liable for the negligence of the doctor.

Mr. Justice STREATFEILD said that textbook writers were writing of a subject in general; they were not writing of a particular patient, and it was common ground between doctors that something must be left to the judgment of the doctor on the spot. This doctor did not only have to treat a case of infective hepatitis, but he had a particular patient, this boy, to treat. He had to bear the whole picture in mind. A general practitioner was entitled to use his common sense, his experience, and his judgment so far as they fitted into a particular case. It would be a sorry day for the medical profession if it were to be said that no doctor or surgeon ought to depart one tittle from that which he saw written in a textbook. Any disease which started by being mild could in the end turn out to be serious, but because a case did end seriously a doctor could not be said to be negligent because he did not form the opinion that it would be serious. All the doctors had agreed that the general practitioner in charge of the case was the man in the best position to judge, and that statements in textbooks were no substitute for his judgment. His Lordship could not follow slavishly the views expressed in the textbooks, because he was bound to accept that evidence. Weighing up the evidence, his Lordship could not come to the conclusion that there had been any falling off from the proper standard of care which a practitioner ought to show his patient.

Nor was this a case where the doctor might have made a mistake which was afterwards found out to be an error of judgment. His Lordship would go a great deal further, and say that not only was the doctor not negligent but that he had not made such a mistake: it was the cruellest misfortune that despite all indications to the contrary the disease turned out to be so severe. It was impossible to find the doctor guilty of negligence and the action failed.

Holland *v.* The Devitt and Moore Nautical College, Ltd., and Thomas—*Queen's Bench Division:* Streatfeild, *J.*, March 3, 1960. Counsel and solicitors: Kenneth Jupp (Pattersons Snow & Co. for Stapylton-Smith, Prance & Co., Bexhill); Stephen Chapman, Q.C., and G. R. F. Morris, Q.C. (L. Bingham & Co.); L. G. Scarman, Q.C., and Peter Webster (Hempsons).

J. F. LAMB
Barrister-at-Law.

Parliament

Report on Oil Heaters

THE Home Secretary made the following statement on the report by the Joint Fire Research Organisation of the Department of Scientific and Industrial Research and the Fire Offices' Committee on the effect of draughts on the burning of portable drip-feed radiant oil heaters which was published on March 7:

The main conclusion is that these heaters are safe in a house with the outer doors and windows closed, but that all the heaters of this type tested are capable of starting a fire very quickly if exposed to a draught such as can be caused by an open outer door.

Copies of the report have been sent to the Government Departments concerned. Copies have also been sent to the manufacturers, and immediate consultations will be undertaken with a view to the adoption of a safe standard of performance for the future, and of any other measures that may be found desirable and practicable.

Meanwhile, it is important that portable oil heaters of the drip-feed radiant type should not be used unless it can be ensured that they are not exposed to a draught.

Mr. G. R. CHETWYND: Will any attempt be made to withdraw these types of apparatus already in use and to get people to return them for suitable modification at the proper time?—Mr. BUTLER: That is precisely the object of the consultations which we are immediately undertaking.

Noise Abatement Society

On March 4 this Private Member's Bill, with the approbation of the Government, was read a second time. In introducing his Bill Mr. RUPERT SPEIR emphasised that its purpose was not noise abolition, but noise abatement. He admitted that there were some glaring gaps in its provisions, including aircraft, aerodromes, railways, and icecream vendors, but he believed that it would enable local authorities and private individuals to take action in a simple, easy, and cheap form, if anyone caused excessive, unreasonable, or unnecessary noise. The chief provisions of the Bill, he explained, were to make noise a statutory nuisance (by an amendment of and addition to part III of the Public Health Act 1936) and to restrict the use of loudspeakers in the streets.

Sir KEITH JOSEPH, parliamentary secretary to the Ministry of Housing and Local Government, said that the Government had decided to set up a committee to examine the nature, sources, and effects of noise and to advise on what further measures

could be taken to mitigate it. When it had reported, the Government would have to consider whether there was a need for legislation and, if so, what form it should take. The sponsors of the present short Bill would not claim that it was a final word on the problem of noise, but at least it aimed to do something about the more outrageous noise nuisances.

QUESTION TIME

Escape of a Virus

Sir ANTONY HURD asked the Minister of Agriculture, Fisheries and Food whether he had yet received a report on the escape of virus from the Pirbright Research Station.—Mr. J. H. HARE replied: An African type of virus of foot-and-mouth disease was found to be responsible for the outbreak at Worplesdon on Jan. 18. Since this type of virus was present at the Research Institute and there is no evidence of the introduction of the virus with imported material, it must be supposed that it escaped from the Institute despite the strict security precautions that are in force. The outbreak was stamped out, and a meticulous investigation has been undertaken by my veterinary staff and the director of the Institute. A thorough review of the stringent disease security precautions taken at the Institute has been completed, but these inquiries have not produced precise evidence of the way in which the virus escaped from the Institute and reached the affected cattle.

Since it must be accepted that an escape took place, it is thought that infective particles which were air-borne escaped through the ventilators of one of the isolation compounds and contaminated the ground in the vicinity, and that thereafter some mechanical transport of the virus took place, probably by a wild animal or bird. The ventilation arrangements for the compounds were designed to confine any escape of virus to the area within the existing vermin-proof fences which surround each unit.

On these assumptions a number of recommendations have been made which have been accepted by the Agricultural Research Council and are being implemented by the Institute. They include further study of the existing ventilation arrangements and the erection of a single perimeter fence which will surround all the isolation units and within which crops attractive to wild life and vermin will no longer be grown. Movements of people and vehicles within the grounds of the Institute are to be reduced by the provision of a car park and bicycle store near the main entrance and the termination of the occupation of two houses which are within the Institute grounds. In this way the risk of contamination of vehicles, workpeople, or wild animal life will be still further reduced.

National Health Service Inquiry

Mr. ELLIS SMITH asked the Minister what representations he had received about the inquiry being held in private into the allegations made about the administration of the National Health Service within the Shrewsbury area of the Birmingham Regional Hospital Board; what advice was submitted by the regional hospital board; what requests he received from the medical consultants within the Shrewsbury area that the inquiry should be held in public; and if an open public inquiry would now be held.—Mr. WALKER-SMITH replied: I have received representations on behalf of individual medical practitioners and from the trades council. The regional hospital board has accepted my decision that the inquiry should be held in private.

Mr. ELLIS SMITH asked the Minister what were the terms of reference of the inquiry appointed by him.—Mr. WALKER-SMITH replied: The terms of reference are:

"To inquire in accordance with Section 70 of the National Health Service Act, 1946, into allegations of irregularities in charging National Health Service patients for medical services in the Shrewsbury area and in particular the allegation that £25 had been paid with a view to procuring admission to a maternity bed at a hospital in Shropshire and to report to the Minister on the facts found."

Oral Contraceptives

Mr. SYDNEY IRVING asked the Minister whether he was satisfied that experimental tests with oral contraceptives being carried out in certain parts of the country were being properly controlled and were safe.—Mr. WALKER-SMITH replied: Limited clinical trials of oral contraceptives are being carried out in this country through unofficial channels, but my information is that they are being carried our under medical supervision and that adequate precautions are being taken for the safety of those participating.

Nursing and Midwifery Staff

In England and Wales in the twelve months ended Sept. 30, 1959, the whole-time nursing and midwifery staff increased by 8010, or 5%, and the part-time staff by 611, or 1½%. In mental and mental-deficiency hospitals the whole-time male nursing staff increased by 1071, or 7%, and the whole-time female nursing staff by 2222, or over 15%. The number of full-time midwives increased by 200, or 3·7%; the number of part-time midwives increased by 51, or 3·6%; the number of pupil midwives increased by 529, or 13·6%.

Public Health

Wolverhampton Night Help Service

Wolverhampton Town Council has decided to introduce a night help service for elderly people who are ill at home. The aim is to provide sitters-in for patients who otherwise would be alone at night, and also (where there is chronic illness) to give relatives occasional relief. That the aged sick should sometimes have to enter hospital simply because they are alone at night is obviously wrong.

The City of Birmingham has had a night help service for some years.

The main difficulty in the Midlands is to attract enough suitable recruits against the competition of industry. In Wolverhampton it is hoped that existing "home helps", on reaching retirement age, will continue as part-time "night helps".

Scattered Cyanide

THE sequel to the accident [1] at Ashby Parva in Leicestershire on Jan. 11, when potassium cyanide fell into the roadway from a haulage contractor's lorry, took place in Lutterworth magistrate's court last week.[2]

The court heard that the lorry had no sides, only side strips about 1½ in. deep, which were "grossly ineffective" for keeping the drums of cyanide in position. There was no back to the lorry platform, to which the load had been secured with tarpaulin sheets and ropes. The lorry driver did not discover that the three drums had fallen off until he arrived in Kidderminster next day. The driver and his employers pleaded guilty to carrying an insecure load and using an unsuitable lorry to carry poison. The driver was fined £20 and the employers £40.

1. See *Lancet*, Jan. 23, 1960, p. 232.
2. *Times*, March 4, 1960.

Infectious Diseases in England and Wales

Disease	Week ended February			
	6	13	20	27*
Diphtheria	2	6	5	3
Dysentery	1433	1578	1670	1667
Encephalitis:				
Infective	..	5	..	1
Postinfectious	2	3	4	2
Food-poisoning	177	261	175	146
Measles, excluding rubella	1580	1551	2806	2131
Meningococcal infection	30	13	20	20
Ophthalmia neonatorum	25	22	12	16
Paratyphoid fever	..	1	3	4
Pneumonia, primary or influenzal	467	508	480	550
Poliomyelitis:				
Paralytic	4	4	5	1
Non-paralytic	1	1	3	3
Puerperal pyrexia	213	179	186	192
Scarlet fever	1208	1193	1201	1226
Smallpox	..	..	..	..
Tuberculosis:				
Respiratory	440	447	499	432
Meninges and C.N.S.	5	6	13	6
Other	42	51	64	51
Typhoid fever	1	4	3	..
Whooping-cough	1037	987	778	856

* Not including late returns.

In England Now

A Running Commentary by Peripatetic Correspondents

THE first signs of spring come each year from Walker's Galleries in Bond Street; for the Medical Art Society puts itself on display just now, and the pictures, being the products of the spare and relaxed moments of a profession usually engrossed in serious realities, tend to reveal the brighter side. But there is a wintry discontent in Jacques Spira's *Prison* and worse in Jakub Rostowski's concentration camp *Fear*—and originality in both. The spring feeling arises from the many competent water-colours which carry our thoughts to clear sky and tempting water—as in *Quay House*, *Blakeney* and *Storm Over Mount Plenay* by R. H. Rushton, *Provence Landscape* by T. Holmes Sellors, the Dufy-like *Leigh-on-Sea: Catamarans* and *Leigh-on-Sea: Boats* of G. H. Rose—to mention only a few in a room dominated by Tom Anderson's lovely vision of the Cam in *The Punt* and to a lesser extent by the ghostly chiarascuro developed under the unpromising title *West Door, St. Albans Cathedral* by H. B. Hewitt.

There's a weight (those who have seen the picture will wince at the pun) in Emanuel Miller's *Church at Sestri Levante* in the oil section and more Dufy there, appropriately at the *Yacht Club, Deauville* by R. A. Beaver; and in the recent development of Frank Forty's style in *Nazare, Portugal* and *Sesimbra, Portugal* there is a suspicion that he, too, next year will have joined the ranks of those under Dufy's influence. W. G. Scott-Brown repeats his Edinburgh success with *West India Dock "Against Wind and Tide"*. As befits an officer of the society, A. M. Rackow has produced a beauty in *On the Common*, and A. B. Hewlett is his usual charming self in *Dampniat*; this latter-day Douanier has undoubtedly arrived at finality in his development. Meanwhile Phoebus Tuttnauer shows the latest stage of his artistic growth in the beautiful *Menorah* and its antecedents in *Trees*.

The atmosphere is there in *Rain* by B. Lux (April showers no doubt), and we only have to turn to W. P. Kennedy's *Chelsea Garden* to feel dry and warm again; for those with a taste for inner warmth there is Vat 69 in *Still Life* by Kathleen Lane. Of portraits there are few, but *Dr. Ian Puddifoot* must feel pleased with René Puddifoot's ability. B. N. Brooke's *Mrs. G. C. Brooke* is deft without being facile; the colour is sublimated in the importance of the drawing, exaggeration of the subject's left shoulder enhancing the head. His *Cat's Eye* shows the mysticism one expects of this artist, but the treatment is in advance of that in earlier pictures. A corner has developed in horses: Geoffrey Konstam has cast a striking *Horse's Head*, while A. Phillips takes the animal as a whole in *Rearing Horse*. And behind them are four garish horses of *The Apocalypse* in oils by Gerald Moore. A. Phillips also takes to stone in *Maternité*, which is good in idea but less skilled in execution.

The society has reached its 25th anniversary; this is its 18th exhibition. Is the show better than before? To many it seemed so. The general level of technical competence has improved; the degree and quality of artistic perception remain the same and are likely to continue so over the years.

* * *

Starlings are the scallywags of the bird world. There's a swagger about their walk and a roll to their shoulders rather like the spiv boys in the heyday of rationing. I feel they should wear dented top hats, tattered white gloves, and carry a black cane. The effect would be heightened by a bent cigar. If they could talk, I can imagine one slowly pushing his hat over one eye and saying "Listen Bud, wanna buy a haystack". And I should know that he had no haystack, and he would know that I knew, and we would both laugh uproariously at this example of sheer rascality.

* * *

When John and I meet we inevitably exchange reminiscences of our student days. There is one memory, however, which we do not need to mention: it is part of us.

It was my first day at the medical school: the first lecture was to be in the physics building at 9 A.M. Outside the door of the lecture theatre there was a press of students, loudly competing for precedence. I remember having the feeling of being an outsider: that all these people knew each other (utter rot, of course). There was one chap, though, who was leaning on a radiator. I went over and leant beside him. "Bit of a scrum," I remarked. "Yes," he replied, "let's wait till it's over." We did, and went in together at the end of the queue. The lecturer was taking names and allotting seats. Seeing us talking, he asked: "Would you two friends like to sit together?" Of course we said yes. So we sat side by side for years, except when some disaster occurred, such as John getting through anatomy at the same time as I passed physiology.

Everyone agrees that there is a moral to be drawn from the story of our meeting and friendship: the trouble is to be sure which moral is correct. John and I have always believed, deep down, that it shows evidence of our innate restraint—even modesty. Our more cynical acquaintances are so unfeeling as to remark pertinently that it was not only at the beginning of our student careers that we constituted the tail-end of the queue.

* * *

It's all very well for the M.R.C. to report that the risk to health of bathing in sewage-polluted sea-water can be ignored, but have they been to Blankport lately? And have they seen the sociologically interesting flotsam at Flocktown-on-Sea this season?

The little world of Public Health is still having quite a time over this affair. The scientists, aloof, objective (and anosmic), have put sundry seaside councils in the clear, and grateful ratepayers are heaving sighs of uncomprehending relief. "Leave it be, Alfie—you don't know where it's been but the M.R.C. says it won't hurt you, not for all practical purposes anyway."

How about that village water-supply at Little Muddlecombe? 50 fæcal coli per ml.? What are you bellyaching about? Has anyone been proved to have caught typhoid from it—yet?

Those bucket-closets at Late Starting? We know they bury the contents round the well, but where's your evidence that anyone is a penny the worse for that? You want the council to spend £20,000 on a drainage scheme? Be your scientific age, old man.

As for your precious slum-clearance schemes, where did you get the notion that unfit houses were unhealthy? You must show proof, you know. Now be a good chap and shut up while we get on with our plans for the new town hall.

* * *

Last month, in a state of apparent Pilkington-unawareness, hospital boards were busy circulating a consolidated edition of the *Terms and Conditions of Service of Hospital Medical and Dental Staff* (*England and Wales*). The accompanying letter of one board was addressed to: "All consultants, S.H.M.O.s/S.H.D.O.s, senior registrars, registrars, J.H.M.O.s and Sessional Bleeders".

* * *

The Lancet minds its P's and Q's
All vulgar error it eschews.
It sticks to doctors' views and news
Both light and solemn.
Yet recently *The Lancet* said
That rabbits, this is what I read,
Might sicken with, till partly dead,
Myxomatosis.
A rabbit with "less lethal form"
Departing somewhat from the norm
In part resists a viral storm
That's semi-fatal.
Since Einstein's day an absolute
By relativitists astute
Is altered, or made quite dilute,
For naught is certain.
Despite the hemi-semi view
The Lancet can't cut death in two
For black or white, not grey or blue,
Are fatal troubles.

Letters to the Editor

PLACENTA PRÆVIA

SIR,—One hesitates to criticise statements made on this subject by one so renowned as Professor Macafee. His advocacy of the expectant management of placenta prævia in 1945 must surely be one of the great advances of post-war obstetrics. Yet he has not strengthened his argument against soft-tissue placentography merely by taking a bald statement out of its explanatory context.

In his article of Feb. 27 he quotes us as saying: "In non-toxic accidental hæmorrhage, once placenta prævia has been excluded and bleeding has ceased, the patient can be safely sent home". This is a correct quotation, but it does not go far enough. Further reading would have shown him in fact that this was not our policy, for we drew attention to the extra risk the fœtus seems to run in some cases of unexplained antepartum hæmorrhage, pointing out however that the hazard was half that of placenta prævia in our experience, not greater as in Professor Macafee's. The cases of minor antepartum hæmorrhage to which *we* refer were patients who had bled so slightly as hardly to amount to antepartum hæmorrhage, yet in whom clinically placenta prævia could not be excluded. When soft-tissue placentography showed a normally situated placenta and all else found normal such patients were allowed to go home. Even so we pointed out the average stay in hospital was eleven days. This practice in our experience has proved safe for mother and child for it is not in these that the fœtal risk is higher. We did not lose a single fœtus in such cases but only in those patients in whom the bleeding persisted so that the patient had to be kept in hospital. That is the subtle difference.

If Professor Macafee's figures showed a significant improvement over ours in the chances for the fœtus in these cases, nothing but good could be said for keeping all such patients in hospital; but they do not—rather the reverse.

It seems obvious, therefore, that we are referring to two different clinical conditions—we on our part to the single insignificant incident and he to the repetitive and more serious one.

Being mindful how misleading statements out of context can be, we hesitatingly draw attention to what Professor Macafee himself has said: ". . . the differentiation between non-toxic accidental hæmorrhage and hæmorrhage from placenta prævia is of little practical value at this period of gestation, since the patient should in any case be retained in hospital for investigation and observation". This surely does not lie comfortably beside what he said originally about the expectant management of placenta prævia in 1945. He said then that patients with suspected placenta prævia, if they were primigravidæ, could safely be sent home as long as no digital examination was done and they lived near hospital. To most practical obstetricians the risk in the latter type of case is incomparably greater than in the one in whom placenta prævia has been excluded. Alternatively we cannot see how he differentiates clinically between these conditions to allow such different management.

In referring to the discussion on soft-tissue placentography at the Royal Society of Medicine in January, 1959, Professor Macafee did not mention some very important issues which were considered. He was silent on what was said about the part soft-tissue placentography could play in diagnosing placenta prævia *before the patient has bled*, and about the proven difficulties of relying on abdominal palpation alone either to diagnose placenta prævia or to exclude it *even with placenta prævia of major degree or entirely absent*.

We have always maintained that soft-tissue placentography is an aid only to the clinical management of placenta prævia and antepartum hæmorrhage, and not something, as Professor Macafee infers, that we suggest should be used as a routine procedure. But we hasten to point out that if by its use placenta prævia can be diagnosed either earlier or more safely or excluded, and in such cases liberate important beds for the better antenatal care of such important conditions as toxæmia, then the case for the intelligent use of soft-tissue placentography surely has been made.

ROBERT PERCIVAL
STANLEY MURRAY.

The London Hospital, E.1.

PRIVATE PATIENTS IN THE NATIONAL SCHEME

SIR,—I find it most perplexing to read the many views about private patients and their drugs. In this practice we are in no doubt. My present partner came in about 6 years ago and one of the reasons we were attracted to each other was that we shared the same views on this matter.

There are only two kinds of treatment, the correct and the incorrect. When a patient comes to us and intimates that he wishes to be "private", we therefore say, "Whatever for?" He may reply that he wouldn't like to be on the N.H.S. list because he wouldn't be getting a satisfactory service. I once had an assistant who told a private patient that he would be expected to attend for consultation at the surgery if his case required it, in the same way as a panel patient—i.e., that it was a medical distinction, not a social one. The patient came to me and complained and was surprised to find that I agreed with the assistant. So when the private patient is asked why he wants to be private, he is reduced to stating that it is on "social" grounds. After all, there couldn't be any medical difference between his case and that of a person in a lower income bracket—a microbe is a microbe, a murmur a murmur, whoever has it. And therefore a doctor is descending to the level of the private patient's snobism, if he condones it.

Now, of course, if he wants to treat everybody, irrespective of class, he will have to work at the highest level, which of course is what we want. For example, if a single-handed doctor working in a closed community, isolated by the nature of the terrain, provided poor accommodation and equipment he would *have* to visit his better-off patients, because they wouldn't tolerate him otherwise. But once you have provided a standard that anyone should be satisfied with, you are no longer at the beck and call of him who cares to get a ten-shilling note out of his pocket.

Now there is nothing, so far as we can see, about the N.H.S. that prevents a doctor from giving first-rate service. We often read of the frustrations of general practice and the obstacles to good work and so on. We don't meet them. Moreover, the old obstacle, lack of money for private fees, no longer exists. And in this practice, hundreds of patients who would in other areas be "private" because of their social status, are quite content to be treated as panel patients, quite happy to attend at the surgery and, if anything, much more considerate than many "panel" patients.

So now we come to drugs for private patients. The drive for this is simply a drive for increasing private practice. So far, I have seen no letters from *patients* demanding their rights—only from doctors indignant for their patients' wellbeing. In this practice we shall continue to encourage the "private" patient to accept our N.H.S. work, which we strive to do to the best of our ability. To do otherwise, is to admit that part of one's work is unsatisfactory, that one gives one standard to one patient but a higher one (for gain) to another, which we consider undignified. And in the sense that a drive for "drugs for private patients" is a drive for "increasing the field of private practice", it would, if successful, reduce still further the time left over for the "panel", with deterioration in that service. A superlative service for the few, at the expense of a poor service for the many is unthinkable and unnecessary.

G. A. STANTON.

Kibworth, Beauchamp,
Leicestershire.

SIR,—I have just seen your annotation concerning private patients in general practice and the interesting assortment of letters on this subject published a week later.

My partner and I are in private general practice (with the exception of a " restricted " N.H.S. list for one school and a small amount of maternity work).

I would question your assumption that if an N.H.S. general practitioner could obtain drugs under the Scheme for his private patients that the result would necessarily be bad for general practice as a whole, by creating " two standards " of medical care. Dr. Soltau (Feb. 20) has pointed out that this cynical view does not exist in Bristol, and I should think the same can be said of most other parts of the country. No " proof " can be offered on either side.

It is an equally reasonable assumption that there would be an *improvement* in the standard of N.H.S. general practice if the numbers of private patients rose. The practitioner would be able to maintain his income at its present level from a smaller total number of patients, if a significant proportion were paying him fees. As a result he would have fewer trivial calls on his time, and more time to devote to practising a good standard of medicine amongst all his patients, private and N.H.S. The real aim of good practitioners today is to have time to work well and not merely to have more money for the same rushed working conditions.

What worries most patients about N.H.S. general practice today is this lack of time on the part of the doctor to listen and to examine thoroughly, and, as a corollary, the lack of personal relationship with his doctor. Here it should be noted that the benefits of " group practice " may be considerable to the doctors concerned, and in some respects to the patients also, but the *individual* patient may find it very difficult to know " his doctor " well, let alone be certain of seeing him in an emergency. It is also a hard fact of human nature that a man values something for which he has paid for voluntarily and personally, rather than by taxation.

From this argument the conclusion can be drawn that it would be far better for the N.H.S. remuneration to be organised on a fee-for-service basis, with some contribution by the State. (Increases in the capitation fee or ingenious methods of " weighting " smaller lists do nothing of themselves to improve the relationship between doctor and patient.) This is a method which works well for both doctor and patient elsewhere—e.g., New Zealand.

Such a sweeping reorganisation would be political dynamite now, but I believe that an extension of private general practice would enable such a change to be considered more dispassionately in the future.

Ipswich. R. H. O. PARKER.

SIR,—I am deeply disappointed at your attitude towards private practice revealed by your annotation of Feb. 13.

Before making things more difficult for the few of us who still limit ourselves to this work, a little thought on the motives that guided us might be profitable. I feel very confident that the great majority of my colleagues are men who took up medicine in the first place as a calling rather than a means of livelihood, and financial considerations did not enter into the matter at all. As Dr. Howard so aptly puts it (Feb. 27), we prefer to be " financially straitened with a clear medical conscience rather than financially solvent with an uneasy medical conscience ".

Without in the slightest degree disparaging our colleagues in the N.H.S., the majority of whom do a first-class job of work under extremely difficult conditions, we probably feel that we ourselves could not keep up the old standards of good family practice that we were trained to perform, and in which treating the patient was just as important as treating his disease, if we had to deal with the very large numbers that an N.H.S. practice involves. To my mind, real family doctoring is the essence of good general practice, and I love to find myself treating the present generation of families that have been cared for by my own family for four generations.

No-one seems to object to an N.H.S. patient seeking consultant advice in private, so why on earth should there be any objection to our much smaller " fees for service " ?

What possible harm private practice can do to the N.H.S. I utterly fail to see, and I certainly don't plead guilty to " perpetuating the defects of ordinary medical care ".

I should like to suggest that your editorial staff should read Philip Auld's book, *Honour a Physician*, which might give them an insight into some of the problems of practice.

A little encouragement to those of us who try to uphold the traditions of good medical practice as it used to be, often at considerable financial loss to themselves, would be more becoming of a leading medical journal.

Wolverhampton. F. H. COLEMAN.

SIR,—" Is a domiciliary visit really necessary for tonsillitis ? " Dr. Smith (March 5) raises a series of issues regarding domiciliary visits. One would like to go into the heart of the matter. I can only recount my personal experience during the past 12 years as a general practitioner here.

Why are domiciliary-visit figures inflated? The obvious answer is because, in the first instance, G.P.s ask for them. But why do they? Mainly because the patient demands this of the general practitioner, and he, in his turn, to keep a satisfactory " clientele ", falls in with the patient's demand. Secondly, it is one of the means of getting a patient into hospital more quickly.

I know of quite a few patients who have changed to another doctor because I did not accede to their " demand " to call in a consultant at home. This has applied not only to children with enlarged tonsils but to adolescents and adults who, though they had been referred to hospital for an outpatient appointment, had been kept on the waiting-list for admission for a considerable time.

The consultant, of course, is pleased to do these domiciliary visits. But call him during the night, as I have, and the first thing I am told is, " I have done my quota. Try another consultant." On trying another consultant I have been told, " I have completed my quota " (in this case he did come the following day).

Recently I asked a consultant to do a domiciliary visit. This particular patient had been under his care as an inpatient on three different occasions for the same complaint. To my utter amazement he told me he did not visit this area (a docks area). It seems unfortunate that a consultant could so easily refuse a domiciliary visit. G.P.s have been reported to the local executive councils for lesser " crimes ", and at times heavily fined.

One of the main reasons for calling in a consultant is the resultant quick hospital admission. Many a time on asking for an " emergency bed ", the house-surgeon or the physician has told me that there is not a bed, but I should call in a consultant for a domiciliary visit. The same thing has been suggested on asking for a bed of the bed bureau. One begins to wonder!

I cannot but agree with Mr. Smith's remarks that " if domiciliary consultations carried no extra pay they would very soon be reduced in number to those that are really necessary ".

Swansea. B. N. MAZUMDAR.

SIR,—May I correct a misapprehension of Dr. M. E. N. Smith (March 5)? He states I attempt to uphold fee-for-service system by my stating that it is already built into the N.H.S. (A curious anomaly that is having its effect in undue emphasis on obstetrics in general practice.) However, I was only pointing out that the Editor should

be more careful in finding his way through the Alice-in-Wonderland regulations of the N.H.S.

The latest of these oddities to come to my notice is the requiring of a family practitioner to certify a domiciliary consultation to the regional board: " That a Consultant has seen a ' bona fides ' residential patient in a nursing home."

In other words, the regional board are requiring me, who is not employed by them, to give a certificate to their accountants " that Dr. Physic, F.R.C.P., is an honest man who is not bilking them ". How did the Royal Colleges allow this monstrous insult to their members to be perpetrated! Why do the accountants of the regional board need the written word of a " bottom-rung " G.P. in addition to that of their own bona-fide top-rung employees—the consultants? The wood of N.H.S. administration is indeed delightfully Tulgey!

Burley, near Ringwood, Hampshire. R. HOWARD.

CHILDREN IN POINTED SHOES

SIR,—So long as mothers wear deforming shoes, their daughters will crave to wear them also. Why women want to wear them is a matter for conjecture. Probably the explanation is their desire to appear as rich and leisured women, a motivation similar to that of Chinese ladies in past times who cultivated enormous fingernails.

Bridlington. P. D. H. CHAPMAN.

PREVENTION AND TREATMENT OF BEDSORES BY SILICONE CREAM

SIR,—I should like to comment on the statement by Dr. Kendall (Feb. 27) that a silicone cream containing dienoestrol " is excellent for the prevention of sores when the skin becomes red at the pressure points (and) for superficial bedsores. . . ."

The value of local treatment in the prevention of pressure sores has been overemphasised, because of the generally held belief that the essential pathology of a pressure sore is an ischæmic necrosis which initially involves the skin, and may then progress to successively involve the subcutaneous tissues and muscle. Husain [1] has shown that in an area subjected to pressure there is considerable necrosis of muscle even at a stage where the only clinical finding is erythema of the skin. I have had histological sections made from similar pressure " sores " and these have shown marked muscle necrosis and have confirmed Husain's findings.

The basic cause of a pressure sore is, of course, a reduction in the blood-supply to the tissues of the compressed area. Various factors influence the length of time that ischæmia must be maintained to cause necrosis, but it is probably as little as four hours. Skin, fat, and muscle possess different degrees of resistance to ischæmia, muscle being less resistant than skin or fat. It is often with surprise that, on removing a superficial layer of necrotic tissue, one finds an enormous cavity going down to bone. In some pressure sores a small blister develops and when the skin is removed the underlying tissues may appear healthy. Only too often it is assumed that what is required is some local application to enable the lesion to re-epithelialise and then all will be well. What in fact is required is relief of pressure. Local applications are a useful adjunct and no more. The same may be said for a pressure area which shows no more than local erythema of the skin.

I have no wish to minimise the importance of care of the skin. My object is to appeal for reorientation of ideas on pressure sores. Ideas are never without influence on practice. If the initial injury is held to be localised to the skin, attention and treatment will be focused here; but if it is conceded that necrosis develops in the muscle at an early stage, the application of ointments or spirit to the skin will be seen to be of secondary importance. Turning a patient off his pressure areas in order to apply ointment or spirit to the skin is probably of more importance than the intrinsic value of the local application.

Amersham General Hospital, Buckinghamshire. M. S. PATHY.

1. Husain, T. *J. Path. Bact.* 1953, **66**, 347.

TREATMENT OF INFECTIONS IN HOSPITAL

SIR,—I cannot let Dr. Everley Jones' letter of Feb. 13 go unanswered. He asks is the increase in streptococcal infections widespread? As a pædiatrician, no doubt this comes as a surprise, but to workers in infectious diseases hospitals this is no new thing.

Notification of scarlet fever has been used as an index to the incidence of streptococcal infections for many years. The annual report of the Ministry of Health for 1958, published in November, 1959, states that the total number of corrected notifications of this disease has been higher than it has been since 1954. The exact annual figures are: 1954, 43,026; 1955, 32,619; 1956, 33,103; 1957, 29,547; 1958, 38,853.

With regard to antibiotics and immunity, I would say that the use—especially if indiscriminate—of penicillin or any other antibiotic, mitigates against the establishment of firm immunity by killing off responsible organisms, either totally or partially before adequate antibody stimulation can be developed.

In other words, widespread use of antibiotics might well provide an increase of infection rather than the reverse, including in the case of the streptococcus the survival of type-12 strain whose nephrogenic properties have been well established.

Surely the only reliable method of reducing its incidence would be an actively immunising prophylactic similar to the toxoids of diphtheria and tetanus rather than killed vaccines. As far as I am aware the biological difficulties associated with the isolation of such an agent seem at present—unfortunately—to be insuperable. I would say that few, if any, authorities still recommend the use of prophylactic scarlatinal toxin because it is troublesome to use and its indications are limited to this condition.

Chadwell Heath Hospital, Romford, Essex. I. M. LIBRACH.

DIURETIC EFFECT OF SPIROLACTONE SC-9420

SIR,—The important observations of Dr. Cejka and his colleagues (Feb. 6) on the diuretic effect of SC-9420 (' Aldactone ') over a 9-day period in a patient with heart-disease necessarily failed to emphasise the clinical significance of this compound, because of the brevity of their trial. Our experiences [1] in 8 patients with cirrhosis and refractory ascites, involving 155 days of hospital treatment with the drug after appropriate control periods, showed a remarkable response in every case.

Prior to therapy, sodium excretion was less than 4 mEq. in 24 hours, and neither weight-loss nor a negative sodium balance could be induced by a low-sodium diet or the use of mercurial diuretics, chlorothiazide, and/or prednisone. Aldactone alone had a weak but definite action on body-weight and sodium excretion, but the greatest effect followed the use of the standard diuretics (which had previously been ineffective) in conjunction with aldactone. On this regime, weight-losses in individual patients of up to $5^1/_2$ lb. daily occurred, and these were associated with 24-hour sodium urinary excretions of up to 337 mEq. Subsequent studies (>200 patient-days) have confirmed the efficacy of the drug, and no toxic effect has been observed.

Besides indicating that " resistance " to standard treatment in such patients is to a great extent the result of hyperaldosteronism, which could in part be a response to therapy with sodium restriction and diuretics, rather than a progressive

1. Clowdus, B. F., Higgins, J. A., Rosevear, J. W., Summerskill, W. H. J. *Proc. Mayo Clin.* 1960, **55**, 97.

failure of hepatic function, aldactone treatment may in most, if not all, instances replace the unsatisfactory treatment currently available. This includes the major and unpredictable operations of bilateral adrenalectomy [2] or portacaval anastomosis; the debilitating routine of repeated paracentesis; and the use of amphenone,[3] which is too toxic for routine purposes, or a spirolactone derivative which involves multiple injections.[4] Moreover, long-term studies suggest that aldactone will permit less rigorous restriction of sodium in the diet in patients with ascites.[1] The drug has two disadvantages; the first is a delay of up to 2 weeks before the clinical response is obvious, and the second, a more important consideration, is its present cost.

B. F. CLOWDUS
J. A. HIGGINS
J. W. ROSEVEAR
W. H. J. SUMMERSKILL.

Mayo Clinic,
Rochester, Minnesota.

AUTOTRANSFUSION IN RUPTURED ECTOPIC GESTATION

SIR,—As one of the first people to write on the subject of blood reinfusion in hæmoperitoneum,[5] I beg your permission to add some further points.

The blood in the peritoneal cavity is very valuable, because after a few hours it becomes "packed-cell" blood. I have found counts up to 8 million per c.mm. due to absorption of the fluid elements by the peritoneum.

I would not go so far as Professor Chassar Moir (Feb. 27) in using blood that has been long effused. After blood has been forty-eight hours in the peritoneal sac it is not infrequent for staphylococci (especially the albus variety) or *Escherichia coli* to find their way into it, and in the publication I mention I quoted a case in which the patient had a temperature of 99·2°F forty-eight hours after the acute rupture and before operation. Reinfusion was not done, but eleven days after operation posterior colpotomy was needed to drain a large pelvic collection of foul infected blood. A sign that the blood is unsuitable for reinfusion is that it changes colour to a brownish purple tint.

The best baler is a coffee cup. Three or four layers of gauze should be put over the mouth of the receiving vessel and the gauze soaked in 3·8% sodium citrate solution before starting to filter the blood. One must be careful not to allow antiseptic lotions to drip from the gloves into the abdomen or the container. I used the technique successfully in several cases of ruptured spleen during the war and have used it in ectopic gestation over the past thirty years without any untoward effects.

Newcastle upon Tyne. FRANK STABLER.

BRETYLIUM TOSYLATE IN THE TREATMENT OF HYPERTENSION

SIR,—In their letter of Feb. 13 Dr. Turner and Dr. Lowther drew attention to some of the side-effects they had encountered. In particular they mentioned that 6 patients had complained of weakness, and commented that they had no evidence that it was due to actual muscular paresis.

Boura and Green,[6] working with the rat-diaphragm/phrenic nerve preparation, were able to demonstrate complete abolition of contractions in response to nerve stimulation with 400 mg. per ml. of bretylium in the organ bath, whereas the sensitivity of the preparation to direct muscle stimulation remained unchanged. Topical application of bretylium to the nerve trunk did not depress conduction, indicating that the block was at or near to the neuromuscular junction. In addition, with cats anæsthetised with chloralose they were able to produce respiratory paralysis and inhibition of the response of the gastrocnemius to indirect stimulation with intravenous doses of 15–30 mg. per kg., direct muscle stimulation being unaffected. In monkeys doses of 50 mg. per kg. of bretylium produced ptosis and a diminution in muscular effort.

Boura and Green concluded from their experimental work in animals that neuromuscular block seemed to be the main toxic effect of the drug, and it seems reasonable to suppose that the same effect may be seen in man, especially when doses of 3600 mg. daily are approached.

Department of Pharmacology,
Medical College of St. Bartholomew's Hospital, London, E.C.1. P. D. MULCAHY.

BRONCHOGRAPHY

SIR,—I read with interest the article by Dr. Smith and his colleagues last week. The technique used at Sully Hospital is essentially similar to that described by myself,[1] but is more complex and in the long run must be more time-consuming.

In a series of some 50 bilateral bronchograms that I performed at the London Chest Hospital Country Branch in 1955, I found it possible to dispense entirely with all local anæsthetics, except for the 2% lignocaine ointment smeared on the Jacques catheter, and this was used mainly for its lubricant properties. Laryngoscopy was also quite unnecessary, and with practice a rubber catheter could invariably be passed easily into the larynx, provided the tongue was pulled well forwards, with the patient sitting in the erect position.

I used an oily solution of 'Dionosil' (propyliodone) which gave excellent contrast and no alveolar filling, clearing usually taking place within 24 hours.

The patients subjected to this technique, many of whom had undergone bronchography by other methods, were interviewed afterwards. They were unanimously impressed by its speed, and by the absence of discomfort.

Banstead Hospital,
Sutton, Surrey. J. C. BARKER.

EARLY TREATMENT OF STOVE-IN CHEST

SIR,—I should like to comment briefly on the most instructive article by Mr. Barrett (Feb. 6).

I think a point which Mr. Barrett might well have made is that an early electrocardiograph is almost indispensable to the full assessment of cardiorespiratory function in these cases. I have been asked to see three cases during the past year which illustrate this contention.

The first, a young man of 33 years, after a motor-car accident had multiple rib fractures, massive left-sided intrapulmonary contusion, and a retroperitoneal hæmatoma. Two days after the accident his E.C.G. suggested the presence of anterolateral epicardial damage, presumably due to direct contusion. Adequate doses of a digitalis preparation seemed very helpful in tiding him over the next few difficult days.

In an elderly man, the E.C.G. taken on the day after the accident showed evidence of extensive anterior cardiac infarction involving the entire thickness of the ventricular wall. It was impossible to tell whether the infarction arose from direct trauma, or was the result of the initial shock and hypotension of the accident. I felt that anticoagulants were contraindicated, and he made a slow and somewhat halting recovery.

A robust man of 65 sustained bilateral multiple rib fractures, and X-ray appearances suggested bilateral intrapulmonary contusion. I saw him two days after the accident, when he was still shocked, hypotensive, and cyanosed. E.C.G. suggested posterior ischæmia and there was a sinus tachycardia of 160 per min. Rapid digitalisation reduced the apex-rate to 110 within twelve hours, with considerable immediate improvement in his general condition. Three days later the E.C.G. had reverted to normal, except for a digitalis effect. This rapid reversal of pattern indicates that the E.C.G. changes were due to acute pulmonary hypertension rather than myocardial contusion or ischæmia, the pulmonary hypertension being brought about by a reflex pulmonary vasoconstriction, as suggested by Mr. Barrett.

Bulawayo. J. CHARLES SHEE.

1. *Brit. med. J.* 1955, i, 1031.

2. Marson, F. G. W. *Lancet*, 1954, ii, 847.
3. Summerskill, W. H. J., Crabbé, J. *ibid.* 1957, ii, 1091.
4. Kerr, D. N. S., Haslam, R. M., Read, A. E., Sherlock, S. *ibid.* 1958, ii, 1084.
5. *J. Obstet. Gynæc. Brit. Emp.* 1934, **41**, 768.
6. Boura, A. L. A., Green, A. F. *Brit. J. Pharmacol.* 1959, **14**, 536.

ORAL HYPOGLYCÆMIC AGENTS

SIR,—I read with interest your leading article [1] on this subject. Regarding biguanides, it mentions only the American works about phenethylbiguanide. May I be permitted to quote the extensive experimental and clinical work which shows the interest and clinical advantage of N N-dimethylbiguanide hydrochloride?

(1) It is particularly well tolerated by the digestive tract; and, if given in divided doses after meals, the digestive side-effects stop the treatment in not more than 1–4% of cases (compared with 15–40% mentioned in the articles on phenethylbiguanide).

(2) Of the many thousands of patients treated with N N-dimethylbiguanide without insulin, there have been no reports of ketosis. On the contrary some antiketogenic activity was noted.

(3) Trials are being conducted in Britain at present. The very extensive work done in France shows a wide range of activity of N N-dimethylbiguanide in every sort of diabetes. Especially in brittle diabetes, the fluctuations in blood-glucose are suppressed. It is often possible to cut insulin in insulin-dependent diabetes. Some action was noted even in diabetic children. The proportion of overall successes is greater than with the sulphonamides.

(4) Three years' extensive experimental work on animals preceded clinical use of N N-dimethylbiguanide, and showed that the drug had negligible toxic effects in therapeutic dosage (calculated on a weight basis).

In man, there was no case of kidney, liver, or blood damage, even after over two years' treatment in more than 10,000 patients. The drug was given without inconvenience to diabetics with sulphonamide jaundice, and to patients with mild azotæmia.

Argenteuil, Seine-et-Oise. JEAN STERNE.

CONTROL OF ANTICOAGULANT THERAPY

SIR,—Dr. Laurie (Jan. 23) concludes that the price of the thrombotest reagent "if sustained, renders an otherwise quite admirable preparation uneconomical for general use".

The original technique requires 0·5 ml. of reagent and 0·10 ml. of blood. The price is then about 1*s.* 6*d.* per test. This technique was devised to secure maximal accuracy and reliability in inexperienced hands. However, we have recently found that the average technician after some training obtains the same accuracy by using only 0·25 ml. of the reagent and 0·05 ml. of blood. Figs. 1 and 2 give the results of simultaneous estimations, using 0·5 ml. and 0·25 ml. of reagent with both capillary and venous blood. The clotting-times agree closely, and the test can therefore safely be used with only half the volume of reagent which was originally suggested.

Besides bringing the price per test down to about 9*d.*, the new technique also has the advantage of facilitating the collecting of the capillary blood samples because of the reduced volume. Our standard interval between controls of patients on long-term anticoagulant therapy is 4 weeks. The cost of thrombotest reagent for one year's treatment consequently is 9*s.*

1. *Lancet*, 1959, ii, 1129.

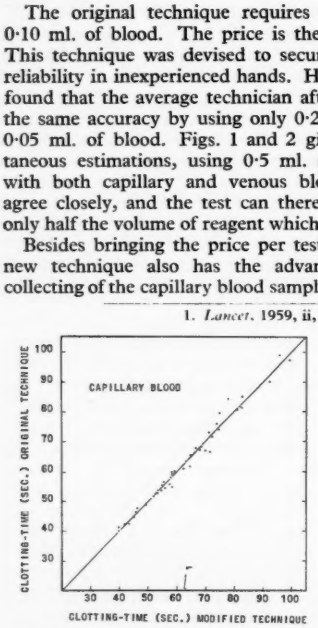

Fig. 1—Comparison of techniques with capillary blood.

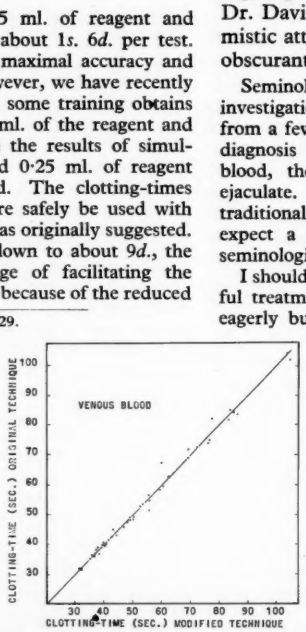

Fig. 2—Comparison of techniques with venous blood.

Rikshospitalet, Oslo. P. A. OWREN.

MAGNESIUM DEFICIENCY FOLLOWING MASSIVE INTESTINAL RESECTION

SIR,—Dr. Fletcher and his colleagues (March 5) have made the interesting observation that the serum-magnesium level was subnormal in a patient subjected to intestinal resection. However, we are uncertain whether they are correct in assuming that the clinical response in their patient was due to treatment with magnesium.

The first fæcal fat excretion of 50 g. per day suggests that the patient was initially receiving considerably more than 50 g. daily in the diet. The fæcal fat excretion of 10 g. per day *after* treatment is taken to indicate that there had been an improvement in intestinal function. This conclusion is only valid if the dietary fat remained unchanged throughout the entire period of study. Patients who have steatorrhœa associated with lesions of the distal small intestine—either resection or regional enteritis—often take high-fat diets in vain efforts to "fatten themselves up". Such patients may improve dramatically when treated with a low-fat (less than 50 g.) and high-protein diet. It is therefore necessary to inquire how much dietary fat was given to the interesting patient described by Dr. Fletcher and his colleagues, and whether fat ingestion had been excessive before admission to hospital.

Postgraduate Medical School, London, W.12. C. C. BOOTH
A. E. READ.

POSTCOITAL EXAMINATION OF SEMEN

SIR,—My purpose in questioning [1] the ultimate usefulness of the usual methods of semen examination was to stimulate discussion which might answer my questions: am I doing the best thing for my patients by adhering to the postcoital urethral specimen, or would I achieve higher pregnancy rates by changing over to masturbation? Dr. Davidson (Jan. 2) is deeply perturbed by my pessimistic attitude, which must seem to him reactionary and obscurantist.

Seminology always appears to me a sledgehammer type of investigation. While cytologists can give useful information from a few desquamated cells, and hæmatologists can make a diagnosis by micromethods instead of demanding a pint of blood, the seminologist must still have the whole sorry ejaculate. If the hæmatologists are willing to abandon the traditional absolute indices as being of little value, might we not expect a similar agonised reappraisal on the part of the seminologists?

I should be grateful for Dr. Davidson's references to successful treatment of subfertile men. I always read such papers eagerly but have never yet been convinced, and this is not merely for the sake of scepticism but mainly to serve the patient better by discovering where lies the truth. One reference from Farris,[2] a pre-eminent seminologist, will suffice to restate my case. Occasionally his zeal makes our eyebrows rise and our hair stand on end. In one experiment (p. 101) he records the seminal examinations of one man who masturbated on each of 20 consecutive days. While this is doubtless a remarkable achievement on the part of both doctor and patient, it served only to confirm what is common knowledge—namely, that the sperm-count is subject to considerable variation, and therefore higher counts should not necessarily be accepted

1. *Lancet* 1959, ii, 974.
2. Farris, E. J. Human Fertility. New York, 1950.

as therapeutic successes. In another test (p. 48) he made a study of the mechanics of masturbation, scientifically checked by stop-watches. Even this experienced investigator could find no way of improving the semen sample apart from "pituitary irradiation, the partitioned ejaculate, and centrifugation" (p. 161); and as for facilitating conception he finds "there is little hope for the subfertile group" (p. 198).

Dr. Davidson describes very generously his investigations which are much more precise and thorough than my more homely, though happier, methods, but I searched in vain for the evidence, drawn from his enviable series of 12,000 husbands, that he is able to report more successful pregnancies than those who favour a more subtle approach. This essential information he fails to give.

Auckland, New Zealand. H. P. DUNN.

REDUCTION OF SPUTUM VISCOSITY IN CHRONIC BRONCHITIS

SIR,—As Dr. Blanshard observes (March 5) there is often a diurnal variation in sputum viscosity, that produced overnight being more viscid than that expectorated during the day. There is also often considerable daily variation in the viscosity of morning specimens.[1] I found that the viscosity of sputum produced by chronic bronchitics in hospital at hourly intervals for three hours during the afternoon varied by less than 5%. This period was chosen, therefore, for the experiments when it was found that after the aerosol inhalation of a water mist for one hour, there was a mean reduction of sputum viscosity of 21·5%.[2]

Department of Medicine, University of Aberdeen. K. N. V. PALMER.

HIGH PLASMA-IRON IN PORPHYRIA

SIR,—The observation by Dr. Hathorn and Dr. Lamont (Jan. 30) of hypersideræmia in 15 of 23 cases of porphyria in the Durban Bantu is of some interest. We have observed significantly raised levels of plasma-iron in 7 of 12 Bantu subjects with symptomatic porphyria cutanea tarda (P.C.T.).

Liver biopsy specimens were taken in 8, and 6 of these showed heavy deposits of hæmosiderin, while in 2 moderate amounts were present. Radioiron studies, in which the plasma iron turnover and red-cell utilisation were measured, gave results compatible with iron overload in 5 out of 12 subjects.

In a further study, liver biopsies were carried out on 25 Bantu subjects with symptomatic P.C.T. In 22, varying degrees of siderosis were found and in 8 cirrhosis was present.

The interpretation of these results is difficult since siderosis occurs in approximately 80% of Bantu adults. It should be noted, however, that there are several reports in the literature in which hypersideræmia [3 4] or excessive iron deposits in the liver [5–7] have been noted in patients with P.C.T. These reports from regions where siderosis is not common, suggest that the association between porphyria and siderosis may be significant.

The frequency of symptomatic P.C.T. in the Bantu is, however, probably not directly related to iron overload, since it can occur in the absence of significant siderosis. On the other hand, it is quite possible that the derangement in porphyrin metabolism may be the result of some unknown agent absorbed with the iron, or alternatively, iron overload may alter the susceptibility of the individual to noxious stimuli.

In white subjects suffering from the hereditary disease, porphyria variegata (mixed porphyria), characteristic changes in iron metabolism occur during acute abdominal episodes. A study of 12 subjects has shown that the plasma-iron level rises and the percentage utilisation of radioiron for red-cell production is reduced. Although these findings can be interpreted in several ways, they raise the possibility that the marrow uptake of iron is impaired during acute phases of the condition.

Department of Medicine, University of the Witwatersrand, Johannesburg. K. J. KEELEY
T. BOTHWELL
S. KRAMER.

ENZYME-DEFICIENCY HÆMOLYTIC ANÆMIAS

SIR,—The paper by Dr. Houston and Dr. Barlow,[1] dealing with a case of acute hæmolytic anæmia secondary to administration of phenacetin, prompts us to comment on the present status of knowledge about the hæmolytic anæmias induced by chemical compounds.

Clinical observation and biochemical studies of erythrocytes have enabled us to recognise a complex enzyme abnormality of red cells as a fundamental predisposing factor in many acute hæmolytic anæmias induced by pharmacological or vegetable agents.

The main feature of this abnormality is a deficiency of glucose-6-phosphate-dehydrogenase,[2] which seems to be inherited through a semi-dominant sex-linked gene; but it is also revealed by the low erythrocyte content of glutathione [3] and by the extreme susceptibility of glutathione to in-vitro oxidation by several compounds, of which acetylphenylhydrazine is the best example.[4] In the same red cells a compensatory hyperactivity of some enzymes of the glycolytic anaerobic pathway has been also demonstrated.[5] Patients affected by this abnormality generally belong to particular ethnic groups and, more specifically, to some peoples of the Mediterranean area (Sardinia, Spain, Greece, Israel) or to the Negro race.

On the basis of such constitutional predisposition, not only phenacetin, but a great number of chemical substances, in pharmacological or industrial use or of a vegetable nature, seem able to provoke a violent crisis,[6] often with hæmoglobinuria.

In this group we must include certain aniline derivatives, such as sulphanilamide and its own derivatives (sulphapyridine, sulphapyrimidine, sulphathiazole, sulfoxone, thiazosulphone, &c.),[7] acetanilide, phenacetin,[8] antipyrin, probenecid, *p*-aminosalicylic acid; substances with a nitro group in their molecule (nitrofurans, chloramphenicol,[9] and trinitrotoluene [10]); naphthalene and its quinone derivatives; quinine and quinidine [11] and 8-aminoquinoline derivatives (primaquine, pamaquin, &c.).[12 13] Hæmolytic factors also seem to be present in several vegetable organisms, since the ingestion of the fruits or the inhalation of the pollen from *Vicia faba*, *Pisum sativum*, *Hydrargyris fœtida*, &c., have been shown to induce an acute hæmolytic episode.[7 14]

As the red-cell defect in glucose-6-phosphate-dehydrogenase seems to be the determining factor in the onset of acute hæmolysis, we thought it advisable to group all these anæmias under the title "enzyme-deficiency hæmolytic anæmias".

PAOLO LARIZZA
PAOLO BRUNETTI
FAUSTO GRIGNANI.
Department of Medical Pathology, University of Perugia, Italy.

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13. Dern, R. J., Beutler, E., Alving, A. S. *J. Lab. clin. Med.* 1955, **45**, 30.
14. Larizza, P. *Rass. med. Sarda*, 1958, **60**, 319.

IDENTIFICATION OF PROPRIETARY DRUGS

SIR,—About 350 to 400 new proprietary drugs are appearing in this country annually; our card-index collection of these now numbers some 2500 collected over six years.

Many of these have identical chemical compositions and hence a common approved name. Many doctors may not have the time to study the officially approved lists; in such cases, we would be very pleased, as a free service to the medical profession, to give full information of synonyms, official and approved names, and approved international names where applicable, to enable these gentlemen to find their way through this jungle.

Dr. M. A. Phillips and Associates,
Consulting Chemists and Chemical Engineers,
9, Western Road,
Romford, Essex. M. A. PHILLIPS.

A PROPOSED GENETIC THEORY FOR THE PATHOGENESIS OF CERTAIN CONGENITAL GONADAL DEFECTS

SIR,—The recent reports [1 2] of 45-chromosome individuals (XO, chromatin-negative) with Turner's syndrome (gonadal aplasia, dwarfism, and congenital somatic abnormalities) suggest that the lacking sex chromosome (X or Y) contains genes which serve to create a balance for normal development in these categories in the presence of the normal X chromosome and autosomal genes. We postulate that chromatin-positive patients (presumably XX) with the complete triad of Turner's syndrome have a chromosomal aberration (e.g., deletion) of a portion of one X chromosome to account for the lack of sex, stature, and somatic balance manifested in these patients. Chromatin-positive individuals with only gonadal aplasia and dwarfism may have a smaller X chromosome aberration affecting only the sex and stature genes, leaving the somatic genes intact.

With the sex genes of one X chromosome partially lost, we may explain those chromatin-positive individuals with incomplete forms of gonadal dysgenesis who have nests of primordial follicles or hypoplastic ovaries (with or without the other stigmata of Turner's syndrome, depending upon whether the stature and somatic genes are also lost). The genes for gonadal development and stature are probably closely associated on the sex chromosome since individuals with gonadal dysgenesis who are not stunted in growth are reported rarely and we have not been able to find any reported cases of gonadal aplasia associated with multiple congenital anomalies that did not have dwarfism.

A chromatin-positive female with only defective ovarian structure and function has been described with 47 chromosomes (XXX).[3] The impaired balance of sex genes in this XXX combination, produced by non-disjunction of the sex chromosomes, probably accounts for the defective ovarian development in this patient. Likewise the impaired sex gene balance in the XXY combination, recently reported in chromatin-positive males with Klinefelter's syndrome,[4 5] may account for the dysgenetic testes found in these individuals.

A phenotypic female with an XY chromosomal complement (chromatin-negative) has recently been reported as an instance of pure gonadal dysgenesis on the basis of primary amenorrhœa and high urinary gonadotrophins.[6] We postulate the presence of a chromosomal aberration involving the sex genes of the Y chromosome (or the sex genes of the X chromosome if they are found to be needed for appropriate genetic balance with the Y sex genes to form normal testes) to explain this phenomenon. Turner's syndrome in males (presumably an XY chromosome combination) may be explained by a similar chromosomal aberration affecting the stature and somatic genes of one sex chromosome with only a partial loss of sex genes, so that hypoplastic or undescended testes are formed which are still capable of bringing about male differentiation. Male pseudohermaphroditism may be due to a hereditary mutation of the maternal X chromosome which affects or modifies the balance with the Y chromosome sex genes and possibly the autosomal genes after fertilisation. Variable degrees of altered expressivity of the sex genes of the Y chromosome due to differing chromosomal aberrations (deletion, inversion, translocation, crossover) or gene mutations on the X or Y chromosome may be involved in those chromatin-negative males with tubular fibrosis, germinal aplasia, congenital anorchia, cryptorchidism, and low fertility when these have a genetic basis.

The Y chromosome has recently been shown to be the bearer of male fertility in *Drosophila busckii*,[7] and of male determining factors in the mouse.[8] We postulate that the formation of testicular elements in the human is dependent upon the presence of a *functional* Y chromosome or the *functional* sex gene portion of a Y chromosome. The development of ovaries would be dependent upon the presence of the *functional* sex genes of two X chromosomes either in the absence of Y sex genes or in the presence of severely altered Y sex genes. We explain the gonadal defects found in the true hermaphrodite on the basis of crossover or translocation processes affecting the sex genes of the X and Y chromosome at the time of their terminal association in the primary spermatocyte. With these phenomena, both XX and XY offspring could inherit specific genes of the opposite sex to produce effects upon the fœtal gonads which depend upon the amount of crossover or translocation of sex genes, and upon which abnormal sex chromosome eventually fertilises the ovum. Two chromatin-positive true lateral hermaphrodites have been described with an XX chromosome complement (46 chromosomes).[9 10] We postulate that the paternal X chromosome donated Y sex genes, obtained by crossover or translocation, which induced the formation of a testicle. Chromatin-negative individuals [11 12] (presumably XY) have been reported with biopsy studies revealing normal ovarian tissue. These patients may have been examples of the paternal X chromosome sex genes completely replacing the Y chromosome sex genes by the crossover phenomenon before fertilisation. Altered degrees of expressivity of the sex genes on the abnormal paternal X or Y chromosome may account for those chromatin-negative or chromatin-positive individuals with gonadal dysgenesis who have vestigial cortical (ovarian) and medullary (testicular) remnants (a lesser degree of differentiation of the ovotestis).

We suggest that there are closely associated, but separate, sex genes on the X and Y chromosome which influence the development of the gonad on each side. An example of a complete crossover between the X and Y chromosome involving the gene(s) of one side only may be the true lateral hermaphrodite with an ovary or testis on the side influenced by the crossover phenomenon and the opposite gonad being induced by the normal gene(s) remaining on the X or Y chromosome. If a partial crossover or a translocation affects the genes involved with one gonadal site then one might have an ovotestis associated with either an ovary or testis on the other side. If a partial crossover or a translocation affects the genes involved with both gonads then ovotestes would appear bilaterally. If a deletion of a portion of the chromosome involved in the

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2. Fraccaro, M., Kaijser, K., Lindsten, J. *ibid.* p. 886.
3. Jacobs, P. A., Baikie, A. G., Court Brown, W. H., MacGregor, T. N., Maclean, N., Harnden, D. G. *ibid.* 1959, ii, 423.
4. Jacobs, P. A., Strong, J. A. *Nature, Lond.* 1959, **183**, 302.
5. Ford, C. E., Jones, K. W., Miller, O. J., Mittwoch, U., Penrose, L. S., Ridler, M., Shapiro, A. *Lancet*, 1959, i, 709.
6. Harnden, D. G., Stewart, J. S. S. *Brit. med. J.* 1959, ii, 1285.
7. Krivshenko, J. *Genetics*, 1959, **44**, 1027.
8. Welshons, W. J., Russell, L. B. *Proc. Nat. Acad. Sci.* 1959, **45**, 560.
9. Hungerford, D. A., Donnelly, A. J., Nowell, P. C., Beck, S. *Amer. J. hum. Gen.* 1959, **11**, 215.
10. Harnden, D. G., Armstrong, C. N. *Brit. med. J.* 1959, ii, 1287.
11. Ashley, D. J. B., Jones, C. H. *Lancet*, 1958, i, 74.
12. Hutchings, J. J. *J. clin. Endocrin.* 1959, **19**, 375.

crossover occurs, the individual might have an ovotestis on one side and no gonad on the other.

We have used basic genetic principles in an attempt to explain certain human gonadal and somatic defects that have been proven or postulated to be on a sex chromosome basis. We hope that this unified theory may stimulate an approach to the study and understanding of these disorders in the future.

A more detailed presentation of this concept will be published elsewhere.

Long Beach, New York.

SOLOMON I. GRIBOFF
ROBERT LAWRENCE.

KARYOTYPES IN KLINEFELTER'S AND TURNER'S SYNDROME

SIR,—Ohno et al.[1] have recently reported that one but not the other X chromosome is heteropyknotic in the female rat. They point out that the X chromosome derived from the father would form the sex-chromatin body since males, having X chromosomes of maternal origin, are sex-chromatin-negative. If such condition obtains in man one might infer the possibility of unreported aberrant karyotypes.

If some cases of "false" (sex-chromatin-negative) Klinefelter's syndrome and of sex-chromatin-positivé Turner's syndrome are phenotypically similar to their "true" counterparts, they may have similar karyotypes. If sex-chromatin-positive Turner's syndrome has only 45 chromosomes, the single X would be of paternal origin. Conversely "false" Klinefelter's syndrome might have an XXY complement in which both X chromosomes are a maternal contribution.

Pursuing these assumptions, let us consider the possibilities should non-disjunction occur at either first or second meiosis in mother or father. Both the reported 47 chromosome XXY Klinefelter's and the 45 chromosome haplo-X Turner's could result from non-disjunction of the sex chromosomes at the first meiotic division in the father. This would give XY gametes and gametes having no sex chromosome. The former could lead to the sex-chromatin-positive Klinefelter's syndrome while the latter deficient gametes could give rise to sex-chromatin-negative Turner's syndrome, as pointed out by Ford et al.[2] Non-disjunction at first meiosis in the mother might give rise to ova having two X chromosomes or to ova having none. The former ova could eventuate in sex-chromatin-negative Klinefelter's syndrome or in triplo-X females having one sex-chromatin body per nucleus. The deficient ova might give rise to sex-chromatin-positive Turner's syndrome having a single X chromosome, paternal in origin. (The other possibility, with Y as the only sex chromosome, we might assume, with Tjio et al.[3], to be lethal.)

Non-disjunction at the second meiotic division in the mother does not add to the hitherto described possibilities, but in the father it could result in diplo-X and diplo-Y gametes. The former could give rise to triplo-X females having two sex-chromatin bodies per nucleus. Perhaps this is the variety reported by Jacobs et al.[4] The diplo-Y gamete could result in the hypothetical karyotype mentioned in your recent editorial.[5]

One case of euploid sex-chromatin-negative Klinefelter's syndrome has been reported.[2] It would be interesting to hear reports on the karyotypes of further cases of "false" Klinefelter's syndrome and of sex-chromatin-positive Turner's syndrome.

Pathology Department,
Stanford University School of Medicine,
Palo Alto, California.

CHARLES P. MILES.

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5. *ibid.* p. 448.

TELEVISION HAZARDS

SIR,—Your annotation of Dec. 26 presents an informative review of some of the disorders that have been reported to result from television viewing. In order that the list be as complete as possible, I am taking the liberty of providing information on several more conditions which have been attributed to the television pastime, and have been reported in the medical literature.

Sprofkin [1] has described the occurrence of a compression neuropathy affecting the common peroneal nerve and its branches in relation both to therapeutic weight reduction and to the prolonged inactivity of the television posture. Cooper [2] has reported what he calls "television bottom", a state, essentially, of coccygodynia, resulting from extended periods of immobility before the TV screen.

Several cases of suicide have been recorded in mentally unstable individuals after viewing television productions dealing with medical topics.[3]

The impact of TV crime shows on juvenile behaviour is already too well documented to require other than passing mention.

Director of Medical Education,
Seaside Memorial Hospital of
Long Beach, Long Beach,
California.

GEORGE X. TRIMBLE.

TREATMENT OF ADVANCED CARCINOMA OF BREAST

SIR,—We hope our dogmatic statement (Jan. 16) "operation is necessary because X-ray castration does not completely stop ovarian function" was not too misleading. We prefer oophorectomy for its rapidity of action and because it must necessarily remove one source of œstrogenic hormones. X-ray castration can, of course, be effective, and in certain cases may be the method of choice. However, it can fail, particularly if the dose is on the low side.

Kottmeier [4] found active corpora lutea at laparotomy after radiation sterilisation. He has also found that there are greater changes in the F.S.H. levels excreted in the urine, in patients who have had an X-ray menopause than in those who have had a radium menopause. This suggests that the level of the ovarian dose of radiation determines the decrease in endocrine function.

Axel Westman [5] studied the problem in rats and found that an X-ray dose of 3000r is needed to cause histological destruction of the ovary. If 1500r is used, ova and primordial follicles are destroyed, but corpora lutea and interstitial cells are not affected. It is likely that the stromal cells and thecal cells are responsible for some of the relevant hormone production, and Jessiman and Moore,[6] in support of this, refer to "cortical stromal hyperplasia" in patients with carcinoma of the breast. These stromal cells need a high dose of radiation to inactivate them, and we feel it is more disturbing to the patient to treat the ovaries to this high level of radiation than to remove them.

In our own series of 267 cases given X-ray menopauses for menorrhagia, we have 38 failures, using a standard technique which delivers 700r to the pelvis in 2 treatments in five days. These are failures to control bleeding, and in 24 cases they could be explained by fibroids or other associated conditions. However, in 14 cases there appeared to be no explanation except that the ovarian cells in these patients were less sensitive to irradiation.

We realise there is no controlled clinical trial of X-ray castration versus surgical castration in treatment of advanced carcinoma of the breast. In the present state

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2. *Scope Weekly*, Oct. 28, 1959.
3. *J. Amer. med. Ass.* 1958, **167**, 497.
4. Kottmeier, H. L. *Acta radiol. Stockh.* 1947, **28**, 736.
5. Westman, A. *Acta endocr., Copenhagen*, 1958, **29**, 334.
6. Jessiman, A. G., Moore, F. D. Cancer of the Breast. Boston, 1956.

of ignorance of the exact nature of the hormones influencing breast carcinoma, and of their exact site of production, we feel that the certainty of surgical castration is preferable to the uncertainty of X-ray castration.

Radiotherapeutic Centre, Addenbrooke's Hospital, Cambridge. E. M. KINGSLEY PILLERS
DIANA BRINKLEY.

SERUM QUININE OXIDASE

SIR,—Referring to the communications by Roman and Dulmanis [1] concerning the results with Baier's quinine-oxidase activity test for the differential diagnosis of obstructive jaundice and hepatocellular damage,[2] we should like to point out that this test has nothing to do with the determination of the quinine-oxidase activity. Using pure water, instead of the aqueous quinine hydrochloride solution, the same results are obtained. The effect is due only to protein precipitation by dilution with water. Details have been published elsewhere.[3]

Clinical Chemistry Laboratory, Gemeenteziekenhuis Aan de Bergweg, Rotterdam, Holland. A. F. K. BUYS BALLOT
J. B. A. TERLINGEN.

"CRISIS IN NURSING"

SIR,—The other day whilst turning out some files I came across a copy of a letter which I sent ten years ago to the then Minister of Health.

Apart from the date it needs no alteration.

29th March, 1949.

Dear Mr. Bevan,

I have long advocated a plan which would help to solve the problem of shortage of nurses and which I should like to put before you.

The essence of the plan is that nurses should not be drafted from the wards to assist in the operating theatre, but that such assistance should be performed by a specially trained staff just as in the physiotherapy or radiology departments.

Many nurses are peculiarly fitted by temperament and inclination for ward work and dislike having to leave the ward, with its human contacts and human problems, to work in the impersonal atmosphere of the theatre. Such nurses never make good theatre assistants because their hearts are not in their work.

Nevertheless, theatre work has a special appeal to a different type of girl (as the advertisements designed to attract girls to the nursing profession attest) and many of these potential recruits are discouraged by the thought that to fulfil their ambition to assist at operations, they will have to go through what to them is the drudgery of the wards with its bedpans and sluices.

As a result of my army experience, I am convinced that such a general training in nursing is not essential as a preliminary for theatre work. It was possible during the war to train a keen young man into a first-class theatre assistant in under a year.

I shall not here go into more details, but I feel sure that such a plan is practicable although it will raise tremendous opposition from the diehards, and I am sure too that it would attract sufficient recruits for theatre work to relieve hundreds of nurses for work in the wards, which in many instances is more congenial to them. As a surgeon I am especially interested in the efficiency of the theatre team and by making this part of the medical service a special profession, I am convinced that this too will be immeasurably improved.

I am, Sir,

Yours sincerely,

The Rt. Hon. Aneurin Bevan, M.P., Minister of Health, Whitehall, S.W.1. H. J. B. ATKINS.

The only official reaction to this letter was a gentle rebuke from the authorities because it was written from the hospital which I have the privilege to serve and might on that account have been regarded as representing the views of that hospital. I hasten to add therefore that so far as I know this letter does not represent the views of the Garrick Club.

H. J. B. ATKINS
Dean of the Institute of Basic Medical Sciences.
The Garrick Club, London, W.C.2.

1. *Lancet*, 1959, ii, 90.
2. *Klin. Wschr.* 1958, **36**, 569.
3. *ibid.* 1960, **38**, 180.

ANTI-SMOKING CAMPAIGN

SIR,—May not the failure of this campaign be due to the fact that its advocates frequently talk a deal of nonsense—for example, that smoking tobacco is on "all fours with smoking opium or hashish"? I have been smoking for 40 years and have never had the slightest trouble in giving it up for a week or so—after a cold, for example. After an attack of "Asiatic" influenza 2 years ago the taste and smell of tobacco became unpleasant to me, and deeply I regret it. I only hope I don't lose my taste for port or claret. I like them both but am not addicted to either.

Buxton, Derbyshire. F. A. BEARN.

WHAT IS A TRANQUILLISER?

SIR,—The definition by Dr. Cook (Feb. 27) is a bit on the sour side, is far from complete, and suggests that chlorpromazine is excluded from its application. I do not presume to offer a definition, but I suggest the addition of the masking of physical signs so that physical disease may escape early recognition.[1]

The earliest description in accord with our notions of what constitutes a tranquilliser which I have been able to discover is that of De Quincey [2] who, referring to opium, spoke of "subtle powers . . . (when judiciously regulated) (1) to tranquillize all irritations of the nervous system; (2) to stimulate the capacities of enjoyment; and (3) under any call for extraordinary exertion (such as all men meet at times), to sustain through twenty-four consecutive hours the else drooping animal energies . . .". Has it been bettered?

Gaillimh, Ireland. S. UA CONCHUBHAIR.

ANTIMONY DIMERCAPTOSUCCINATE IN INTESTINAL BILHARZIASIS

SIR,—In their interesting letter [3] on the suppressive management of urinary bilharziasis with antimony dimercaptosuccinate (TWSb), Dr. Friedheim and his colleagues have demonstrated the promising effects of a single intramuscular dose, which have been confirmed by Friedheim and de Jongh.[4] Recently a small experiment on similar lines was conducted in East Africa on the intestinal form of the disease (*Schistosoma mansoni*).

16 patients from an endemic area of *S. mansoni* near Nairobi, Kenya, were divided into two groups of 8. None had received previous treatment. The sole criterion was that they should be passing many viable ova, easily visible on direct stool microscopy. The first group received a single intramuscular injection of TWSb. The second group received two intramuscular injections on successive days. Dosage was calculated on a sliding scale dependent on body-weight: 15–25 kg., 300–350 mg.; 26–36 kg., 350–400 mg.; 37–49 kg., 400–450 mg.; 50 kg. and above, 500 mg. The drug was given in 10% solution dissolved in sterile normal saline. Fæcal examinations were carried out frequently by direct microscopy and the hatching test described by Newsome.[5] 6 patients from each group of 8 were satisfactorily followed up for five to six weeks. In 5 of each group, egg excretion was impaired for two to four weeks, beginning seven to ten days after administration of the drug. In 1 of each group no effect on egg production was demonstrable. 6 of each group (i.e., all who completed follow-up) reverted to their pretreatment egg output within thirty-eight days after dosage. This was confirmed by a check examination on the fortieth day.

In this small experiment, the dosage of the first group was

1. Ua Conchubhair, S. *J. Irish med. Ass.* 1959, **44**, 117.
2. De Quincey, T. The Confessions of an English Opium-eater, 1821–22.
3. Friedheim, E. A. H., Salem, H. H., El Sherif, A. F. *Lancet*, 1959, ii, 410.
4. Friedheim, E. A. H., de Jongh, R. T. *Ann. trop. Med. Parasitol.* 1959, **53**, 316.
5. Newsome, J. *Trans. R. Soc. trop. Med. Hyg.* 1951, **44**, 611.

similar to that employed by Friedheim et al. The second group received twice the dose given to the first group, but egg production was only affected for some two to four weeks. All patients had strongly positive hatching tests at thirty-eight days, whereas the *S. hæmatobium* patients of Friedheim were still not passing any viable ova at one month.

It appears that the encouraging results of suppressive management of urinary bilharziasis cannot necessarily be applied to the intestinal form of the disease. The effect of TWSb injections repeated monthly is now being studied in patients with *S. mansoni* and *S. hæmatobium* infections.

Medical Research Council
Bilharzia Research Group,
Medical Research Laboratories, Nairobi. A. DAVIS.

GENERALISED LYMPHADENOPATHY, BLOOD CHANGES, AND RASH ASSOCIATED WITH METHOIN

SIR,—Since the introduction of new anticonvulsants (such as phenytoin, methoin, and troxidone) there have been many reports of toxic manifestations,[1–8] the most significant reactions being hæmatological. During treatment with 5-ethylphenylhydantoin (' Nirvanol '), which was once used for rheumatic chorea, a mild lymphadenopathy was noted[9]; and it is now recognised that hydantoin can cause generalised adenopathy of varying degree, mimicking clinically and pathologically a malignant lymphoma.[8 9]

Salzstein and Ackerman[10] collected from the literature 82 cases of lymphadenopathy induced by anticonvulsant drugs, particularly by methoin. The cervical nodes are often involved. The glands are often tender, and they usually first appear one to two weeks after treatment began, or may be very much later. Although lymphadenopathy may be the only toxic manifestation, it is usually associated with other reactions, such as fever, skin rashes, hæmatological changes, and liver involvement. The most characteristic feature of this lymphadenopathy is its disappearance when the drug is stopped. When biopsy was performed the nodes showed reticulum-cell hyperplasia with many mitotic figures and infiltration with eosinophils, neutrophils, plasma cells, and young lymphocytes.[10–11] Chiari[11] referred to fibrinoid necrosis.

Among changes in the blood-picture leucopenia may lead to agranulocytosis and aplastic anæmia. There is a mild leucocytosis in some cases. Lymphocytosis[12] and monocytosis[11–13] have been reported. In very many cases a significant eosinophilia was found.[10] Increase in plasma cells was noted in 2 patients; and in 2 a typical picture of lupus erythematosus developed after administration of methoin.[14]

The following case may be of interest.

A 38-year-old unmarried female was admitted to hospital because of fever, skin rashes, and lymphadenopathy. Twenty-six days before, high fever and cough developed. She was given penicillin and later chloramphenicol but the fever persisted. During the course of penicillin a generalised morbilliform rash appeared and continued despite stopping the penicillin. In the last few days of penicillin therapy a cervical lymphadenopathy was noted.

She had been in good health until the age of 23 when grand-mal seizures began. In the past six years she was treated with phenobarbitone and diphenylhydantoinate, and the attacks had disappeared. Six weeks before admission, methoin was introduced (0·2–0·3 g. daily).

On admission to hospital she was an acutely ill and mildly underdeveloped female with temperature of 37·8° C (100° F). There was a generalised scarlatiniform rash and desquamation of the hands. Several firm, indolent, freely movable lymph-nodes were found in the cervical, axillary, and inguinal regions. No other abnormal findings and no enlargement of the liver or spleen were detected. X-ray of the chest was normal. The tongue was reddened and the papillæ were atrophied. A diagnosis of idiopathic epilepsy was substantiated by electroencephalography.

Laboratory data.—Red cells 3·7 million per c.mm., hæmoglobin 10 g. per 100 ml., white cells 11,000 per c. mm. (38% neutrophils, 21% band forms, 2% monocytes, 17% eosinophils, 2% plasma cells, and 18% lymphocytes). Reticulocytes 4·5%. Hæmatocrit 40%. Platelets 280,000 per c. mm. Paul-Bunnel, direct Coombs, Widal, and brucella agglutination tests were negative.

Bone-marrow puncture showed an eosinophilic reaction (18·5% eosinophils) and plasmocytic proliferation (10·5% plasma and reticulum cells). Thymol turbidity test 17 units. Total serum-cholesterol 120 mg. per 100 ml., total serum-bilirubin 1 mg. per 100 ml., blood-urea 20 mg. per 100 ml., total serum-protein 6 g. per 100 ml. (albumin 2·4, alpha-globulin 0·12, alpha-2-globulin 0·42, beta-globulin 0·72, gamma-globulin 1·9).

A cervical lymph-node was biopsied (Prof. Besima Tarhan) and showed destruction of most of the normal architecture. A striking reticulum-cell hyperplasia was found. Some lymphoid hyperplasia and sparse plasma cells were present.

After methoin was stopped fever subsided in a few days and the rash disappeared slowly. The lymph-node enlargement subsided completely in twenty-five days. One cervical node swelled again to the size of an egg, but it disappeared in a few days with local treatment. The hæmatological findings on the thirty-second day were: white cells 9000 per c.mm. (64% neutrophils, 12% band forms, 5% eosinophils, 8% monocytes, and 11% lymphocytes). Thymol turbidity test 7 units. All symptoms disappeared and the patient is now fit, apart from occasional epileptic seizures.

Because symptoms appeared during methoin therapy and disappeared completely when it was stopped we feel convinced that methoin was the cause. Possibilities such as infectious mononucleosis, undulant fever, and lupus erythematosus were eliminated; and Hodgkin's disease and benign lymphogranulomatosis were not suggested by the histological pattern of the lymph-node and the disappearance of all symptoms.

As far as we know, only 2 instances of lymphadenopathy induced by anticonvulsant therapy and associated with plasmocytic reaction in bone-marrow have been reported[10 15] (1 with a plasmocytosis of 22%). Some authors have recorded monocytosis in toxic reactions due to hydantoin therapy.[11–13] We believe that the paucity of reported plasmocytosis in lymphadenopathy induced by anticonvulsant therapy is due to the lack of complete hæmatological investigation in the vast majority of cases.

MUZAFFER AKSOY
HALE DEVRIMEL
HAYRETTIN ALPÜSTÜN.
Department of Internal Medicine,
Beyoglu Ilk Yardim Hastahanesi,
Istanbul, Turkey.

A PORTRAIT OF Mrs. HARVEY

Prof. K. J. FRANKLIN writes:

" There used to be at Burley on the Hill a portrait in oils of Mrs. Harvey, wife of the discoverer of the circulation of the blood, but it was destroyed by fire towards the beginning of this century. I should very much like to get a description from someone who saw the picture before its destruction, even more to find a photograph or painted replica of it. I should therefore be most grateful to anyone who can and will send me information (at Broomfield, Yarnton, Oxon.)."

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2. Eaton, L. M. *Coll. Pap. Mayo Clin.* 1952, **44**, 556.
3. Merritt, H. H., Carter, S. *Med. Clin. N. Amer.* 1950, **34**, 341.
4. Kaufman, I. C. *ibid.* p. 1507.
5. Kaufman, I. C., Isenberg, S. *ibid.* 1952, **36**, 1381.
6. Bercel, N. A., Finesilver, B., Solomon, P., Somerfeld-Ziskind, E., Ziskind, E. *J. Amer. med. Ass.* 1950, **143**, 1460.
7. Lennox, W. G. *ibid.* 1945, **129**, 1069.
8. Witkind, E., Waid, M. E. *ibid.* 1951, **147**, 757.
9. Jones, T. D., Jacobs, J. L. *ibid.* 1933, **99**, 18.
10. Salzstein, S. L., Ackerman, L. V. *Cancer*, 1959, **12**, 164.
11. Chiari, H. *Wien. klin. Wschr.* 1951, **63**, 77.
12. Loscalzo, A. E. *J. Amer. med. Ass.* 1947, **135**, 496.
13. Boller, W. *Schweiz. med. Wschr.* 1943, **73**, 699.
14. Lindquist, T. *Acta med. scand.* 1957, **158**, 131.
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Obituary

TOM DOUGLAS SPIES

M.D. Harvard, Hon. Sc.D.

NUTRITION is a part of medicine where the scientist and the humanitarian can usefully support one another. Tom D. Spies was a man who combined the qualities of each, and his studies of deficiency diseases and their treatment especially by synthetic vitamins won him an international reputation. He died in hospital in New York on Feb. 28 at the age of 57.

As a boy in Texas he was shocked by the deaths from pellagra which he saw among the neighbours and when he visited the country practices of his two uncles. At Harvard while still a medical student he made a special study of the disease, and after he qualified in 1927, while he was holding intern posts at Peter Bent Brigham Hospital in Boston and at the Lake View Hospital in Cleveland, he used to spend many hours at the bedside of pellagra patients. He tended them and supervised their diets himself, and by assiduous care he achieved remarkable results. At that time it was thought that the pellagra which was prevalent among the alcoholics of North America was a different disease from the pellagra of the malnourished South, and Dr. James S. McLester later invited Spies to go to Alabama to see whether he could repeat his results there.

Since 1931 Spies had been attached to the teaching staff of the University of Cincinnati, and in 1934 the university gave him leave to spend some months at the Hillman Clinic in Birmingham, Alabama. His first study was to treat 50 pellagrins with the diet he had been using successfully in the North. Under his regime only 3 died, but the cost of the treatment in money and skilled care made it prohibitive for the impoverished people who were the chief sufferers. In 1937 Elvehjem's observation that nicotinic acid cured a case of black tongue in a dog encouraged Spies to use this chemical cautiously and then with growing confidence among his patients. The success of this cheap remedy was remarkable. His work at the Hillman Clinic (where he now spent nine months of each year) greatly expanded. Other synthetic vitamins—such as riboflavine, ascorbic acid, and pyridoxine—were gradually introduced, for Spies recognised that nicotinic acid was not a panacea and that much of ill health of the South was due to what he called subclinical mixed deficiency disease.

The clinic became a centre of controlled research, while Spies and his associates visited the city and rural slums of Alabama, treating not single patients but whole families, sometimes even including the dog. What was in effect a nutritional laboratory on this scale required large funds to support it, but the results of Spies' work were striking and in 1943 a group of industrialists formed the Spies Committee for Clinical Research. With the discovery of folic acid his work spread to Havana, where in 1945 he treated his first 10 cases of tropical sprue —a disease which has now been almost eradicated from Cuba. In the years after the war, some of the studies of his Cuban-American team on vitamin B_{12} in macrocytic anæmias and on the treatment of leukæmia with steroids appeared in our columns.

In 1947 Spies was appointed chairman of the new department of human nutrition and metabolism at North Western University, Chicago, and he continued to hold the chair there, and to act as visiting professor in the University of Alabama. In 1944 he was awarded the honorary degree of SC.D. from the University of the South in Sewanee, Tennessee, and in 1957 the distinguished service medal of the American Medical Association. In Cuba, to which he went as a foreigner, his single-minded devotion to the health and welfare of the people was recognised when the Government gave him the Carlos Finlay medal. He had in fact dedicated himself to his work, disregarding his own prosperity or comfort, and in his long and disabling illness he continued that work with the courage which, like generosity, came naturally to him.

Dr. R. G. ANDERSON

E. O. L. writes:

"Dr. Anderson and I were colleagues as visiting commissioners of the Board of Control for seven years, and later for four years as Lord Chancellor's visitors. In these posts the reliability of one doctor's observations and the soundness of his judgment is of the utmost importance to his colleagues who later may have to deal with the same patient or problem. In these respects I always felt that Dr. Anderson was an ideal colleague. Before seeing a patient he made himself conversant with all relevant information and he would listen carefully to the views and opinions of others; but when he came to examine the patient he made his own observations with meticulous thoroughness and with the utmost objectiveness, unbiased by the opinion of others. His diagnosis and conclusions were based upon his own observations. He was singularly free from the bias of any current professional or scientific craze or fad; and his colleagues placed great reliance on his reports.

"He was a man with a fine presence and radiated geniality. His natural and spontaneous smile was that of a man at peace with himself. More than once I saw him confronted with an aggressive, abusive, maniacal, and paranoidal patient; but it was not long before his courtesy and geniality disarmed the patient. One secret of his success was his patience in listening, even when the patient was irrational. He avoided giving the patient the feeling that he was being observed or being cross-examined. His patients I think felt that Dr. Anderson was a physician who endeavoured to understand their difficulties, views, or standpoints.

"Those who had the good fortune to be his colleagues valued highly Dr. Anderson's general efficiency as a psychiatrist and the dignified manner he fulfilled the functions of a commissioner and Chancery visitor. He was loyal to the best traditions of his profession, and therefore held in the highest esteem by patients and doctors in all parts of our country. To be a colleague of his meant inevitably becoming his friend."

Appointments

BOSTOCK, A. D., M.B. Manc., D.P.H.: senior assistant M.O., Nottingham.

BRAYN-SMITH, ANGELA J., M.R.C.S., D.A.: assistant M.O.H. and school M.O., Denbighshire.

BRISCOE-SMITH, J. H., M.B. Birm., D.P.H.: M.O.H., Westminster.

CROWTHER, J. S., M.D. Lond., M.R.C.P.: consultant chest physician, Nottingham chest clinic and Ransom Hospital, near Mansfield.

EDWARDS, J. W. L., M.D. Lpool, M.R.C.P.: part-time consultant physician, Ormskirk and district H.M.C. group.

GARRETT, GEOFFREY, M.D. Manc., D.PATH.: consultant pathologist, Oldham and district group of hospitals.

LOVGREEN, E. S., M.B. Lpool: assistant M.O.H. and school M.O., Denbighshire.

MARSDEN, A. J., M.B. Lpool, F.R.C.S.: part-time consultant general surgeon, Newsham General Hospital, Liverpool.

PAGAN, R. T., M.B. Lond., D.P.H.: deputy M.O.H. and deputy principal school M.O., Rotherham.

ROHAN, T. M. B., M.B., D.P.H.: M.O.H., Hucknall, Nottinghamshire.

SUTHERLAND, I. B., M.B. Edin., D.P.H.: assistant senior M.O., Leeds Regional Hospital Board.

Notes and News

ST. GEORGE'S MODERNISED

OPENED in 1733 at Hyde Park Corner, St. George's Hospital was rebuilt in the 1830s. A second rebuilding was planned before the late war, but in 1947 a decision was made to transfer the hospital to South London. In 1952 it took over some wards at the Grove Hospital, Tooting, the site finally decided upon, and in 1954 The Grove became part of St. George's. But by that time there seemed to be no hope of building a new hospital at Tooting within ten or fifteen years, and to fill the gap a big reconstruction of the hospital and medical school has been undertaken. Possessing about £1 million in endowment funds, the governors have themselves provided about £400,000, or nearly half the total capital expenditure on their group between 1953 and 1959. But further gifts and the use of their wide powers of investment has left them with £900,000. They now have 318 beds at Hyde Park Corner, 374 at St. George's Hospital, Tooting (formerly The Grove), 104 at Atkinson Morley's Hospital, Wimbledon, and 106 at Victoria Hospital for Children, Tite Street.

Last week the reconstructed medical school was on view. The plan was designed to provide new laboratories for research and routine work in the departments of pathology, chemical pathology, bacteriology, and virology, and to allow for the establishment of clinical units in surgery and medicine. In addition, there has been comprehensive reorganisation of the teaching rooms and improvement of the social facilities. A great part of the old school buildings has had to be demolished, including the octagonal 19th-century library, which has now been replaced by a new building on the site of what was at one time the dissecting-room. In effect, a corridor building has been erected which joins the main entrance to the school in Knightsbridge with a subsidiary entrance in Grosvenor Crescent Mews, and this forms the western side of the main hospital building. The work has been done with a skill which preserves a great deal of the special character of the place.

The school now accommodates professors in the departments of medicine, pathology, bacteriology, and chemical pathology, and leaves room for a professor of surgery at some future date. It is a fitting academic centre for its large and important teaching group.

PROGRESS IN DENTISTRY

LAST Saturday the Guy's Hospital Dental School held its annual clinical meeting. Major developments cannot be expected every year, but nobody can fail to be impressed by the progress made as the result of scientific methods applied to dentistry.

A good illustration is the work being done by Mr. M. N. Naylor in the department of dental medicine on the rate at which thermal stimuli are transmitted through dentine. The results show a wide discrepancy between measurements made in vitro and in vivo, and may eventually help towards answering the still controversial question whether nerve fibrils are contained within the dentinal tubules. A fine example of the possibilities of cine radiography was shown by Mr. W. J. Tulley of the children's department. He has developed a method of taking radiographs (with the help of an image intensifier) of the movements of the tongue, which is coated with a barium emulsion to render it radiopaque. As it is now generally conceded that abnormal patterns of muscle movement are responsible for many cases of malocclusion, such a method could provide a good deal of assistance in planning treatment and in prognosis. Another film shown was that of an osteotomy performed by Mr. D. M. Macdonald for hemihypertrophy of the mandible. This film, produced under the direction of Mr. A. D. Robinson, showed what can be done by cooperation between the oral surgeon and the dental technician in the correction of a distressing facial deformity.

The main lecture of the day was given by Dr. B. Cohen, the newly appointed Nuffield professor of dental science, who spoke on the hazards of radiation in dentistry. It is only within the past few years that the risks to the dental radiographer have been appreciated fully, and, as Professor Cohen pointed out, some operators still hold the film in place themselves—a procedure which it is now realised may have far graver effects than a radiation burn of the finger. It is dangerously easy to forget that radiation is cumulative; the dental patient is unlikely to receive more than a few seconds' irradiation in a lifetime, but the dental surgeon who uses an X-ray machine regularly may receive a considerable dose unless he takes the essential precautions. Investigations at Guy's Hospital on the safest place to stand while taking a dental radiograph show that this varies widely with the teeth being examined; normally, the safest place is behind the tube, but when anterior teeth are being radiographed it is better to stand behind the patient. With the help of a Geiger counter and a small radioactive source, Professor Cohen showed how great a measure of protection is provided by the " inverse-square " law between distance and radiation received. He also demonstrated very clearly how little protection is afforded by ordinary brickwork—a point to be remembered if the X-ray beam happens to be directed at the wall of an adjoining room. As has been mentioned before, all dental X rays should be filtered through the equivalent of 2 mm. of aluminium and the beam should be accurately collimated. Professor Cohen laid stress on the importance of obtaining good radiographs at the first attempt, so that the required information could be obtained without having to subject the patient to an unnecessary second dose of radiation.

In the afternoon, Prof. M. A. Rushton gave his perennially popular talk on the curious and often puzzling cases referred to the department of dental medicine during the year. Although many of the odd conditions are rarely seen and are evidence of harmless congenital abnormalities, there are always the few uncommon but potentially serious diseases, such as multiple polyposis and hereditary hæmorrhagic telangiectasis, which produce pathognomonic appearances in the mouth and which may be recognised by the alert.

BENEFITS FOR LONG-STAY HOSPITAL PATIENTS

THE Minister of Pensions and National Insurance has accepted the recommendation of the National Insurance Advisory Committee [1] on the position of long-term hospital patients under the National Insurance scheme. The most important change proposed is that mental patients who are detained in hospital as a result of criminal proceedings should be treated in the same way as all other mentally (and physically) ill patients, and should cease to be disqualified for National Insurance benefits, and for contribution credits. Where they are admitted to hospital from prison while under sentence, they will, however, still be disqualified until the sentence ends. At present a mental patient who is regarded as detained in legal custody cannot get benefit either for himself or his dependants. Though he is allowed to pay non-employed contributions, they do not count for sickness or unemployment benefits on his discharge from hospital.

The committee also considered the effect of rehabilitative work on the patient's right to sickness benefit. At present a hospital inpatient can earn up to £2 a week from rehabilitative work without forfeiting his sickness benefit. As more than 98% of the hospital patients doing work receive less than £2 a week, the committee recommend that this limit should remain, but they would like to re-examine the position should the employment pattern of hospital patients change substantially. Outpatients, the committee propose, should also be subject to the £2 a week limit, and should show that the work they do is beneficial and, if they are working for an employer, does not exceed eight hours a week.

A patient without a dependant has his sickness benefit reduced to the pocket-money level of 10*s.* a week after a year in hospital. The committee recommend that benefit at the " pocket-money " level should not be paid if, in the opinion of the hospital authorities, it, or some lesser sum, cannot be used by, or for, the patient. Any such benefit should accumulate for a year and be paid to him in the event of his discharge from hospital.

The cost of these recommendations will probably be about £50,000 a year.

1. Cmnd. 964. H.M. Stationery Office. 1*s.* 3*d.*

POSTGRADUATE CONFERENCES IN GLASGOW

FOR the past four years the University of Glasgow and Royal Faculty of Physicians and Surgeons have been holding a series of conferences as part of their postgraduate education programme. The Kidney has been chosen as the subject of the next, which is to be held in the hall of the faculty, 242, St. Vincent Street, Glasgow, C.2, from March 30 to April 1.

It will be opened by Mr. Arthur Jacobs and the speakers will include Mr. W. F. Cook, Prof. Roger Warwick, Dr. A. M. Joekes, Dr. H. E. de Wardener, Prof. A. A. G. Lewis, Dr. M. D. Milne, Prof. D. A. K. Black, Prof. G. M. Bull, Dr. J. W. Chambers, Dr. J. C. Eaton, Dr. F. M. Parsons, Dr. J. S. Robson, Dr. A. C. Kennedy, Dr. I. A. Short, Dr. Molly Hill, Dr. G. C. Arneil, Dr. R. H. Gorrill, Sir Dugald Baird, Mr. Alexander Marshall, Dr. J. D. Williams, Prof. W. S. Peart, Prof. Clifford Wilson, Prof. Ian Donald, and Dr. C. Dollery.

There is no fee for the course. There will be an informal dinner on March 31 (tickets £1). Further particulars were given in our advertisement columns last week.

University of Oxford

On Feb. 27 the following degrees were conferred:

D.M.—R. A. Bruce.
B.M.—D. I. Fry, R. J. Lunt.

University of London

Dr. J. H. Green, senior lecturer in physiology at Middlesex Hospital Medical School, has been appointed to the university readership in physiology tenable at that school.

Triple Qualification Board of Scotland

The following have been granted the diploma of licentiate of the Royal Colleges of Physicians and Surgeons of Edinburgh and the Royal Faculty of Physicians and Surgeons of Glasgow:

D. T. M. Calderwood, M. R. Campbell, K. C. Clarke, G. I. Cohen, David Crookenden, L. C. Florin, N. G. Hamilton, Stella Pak-Ngor Ho, A. S. Jackson, Botio Kalcev, Sybil F. Kinghorn, A. N. Kotwall, E. T. Nagy, W. H. Williams.

Training in General Practice

Three further Nuffield practitioners have been appointed under this scheme (*Lancet*, Feb. 6, p. 343). Dr. W. F. Webb is to be registrar to the Portsmouth Group and later trainee to Dr. M. Duncan; Captain P. P. Carter, R.A.M.C., registrar to the Royal Hants County Hospital, Winchester, and later trainee to Dr. G. Swift; Flight-Lieutenant D. R. Burcombe registrar to the Southampton Group and later trainee to Dr. D. Ramsay.

International Society for Tropical Dermatology

At the organisational meeting of this society in New York on Jan. 25 Prof. Aldo Castellani was elected president, Dr. Frederick Reiss secretary-general, and Dr. J. Lowry Miller treasurer. The inaugural meeting is to be held on May 10, at 8 P.M., at the Rockefeller Institute, New York, when Professor Castellani will give an address on elephantiasis tropica and elephantiasis nostras. Further particulars may be had from Dr. Reiss, 870, Fifth Avenue, New York, 21, N.Y.

Life Insurance Medical Research Fund of Australia and New Zealand

This fund has been established to promote and assist scientific and medical research in cardiovascular function and disease. Grants will be made as follows:

Grants in aid (£1000–£3000) will be given to non-profit institutions with basic facilities and qualified personnel for medical research to be used in support of a specific programme of investigation under the direction of a particular investigator.

Research fellowships in Australia and New Zealand (£2000–£2250) will be granted for one year, but renewal for further periods may be approved.

Travelling fellowships (£2250–£2750) will be granted for a period of two years abroad, followed by a third year in an approved institution in Australia or New Zealand.

Further information and application forms, which should be returned by July 1, may be had from Dr. B. C. Sinclair-Smith, medical director of the fund, 87 Pitt Street, Sydney, New South Wales, Australia.

World Health Day

World Health Day is observed each year on April 7 to mark the anniversary of the coming into force of the constitution of the World Health Organisation in 1948. The theme chosen for 1960 is Malaria Eradication—a World Challenge.

Mr. Terence Cawthorne is to be the guest of honour at the annual meeting of American Laryngological, Rhinological, and Otological Society in Miami on March 15.

The annual general meeting of the Anglo-German Medical Society will be held on Friday, March 18, at 8 P.M., at 41, Portland Place, London, W.1.

Vitamins Limited have some tickets for watching the Boat Race from their premises on April 2. Applications should be sent to 23, Upper Mall, Hammersmith, London, W.6.

Diary of the Week

MARCH 13 TO 19

Sunday, 13th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
10.15 A.M. Mr. S. E. Birdsall: Problems in Otolaryngology.

Monday, 14th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Prof. Eleanor Zaimis: Neurochemical Pharmacology.
GUY'S HOSPITAL, S.E.1
5.30 P.M. Dr. G. A. Thomas: Disorders of Testicular Function.
INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5.30 P.M. Prof. Derek Denny-Brown (Boston): Nature of Brief Recurrent Cerebrovascular Episodes.

Tuesday, 15th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Pathology.* Dr. William Hayes: DNA and Biological Research. Dr. E. J. Holborow: Serum-anti-nuclear Factor and Autoimmunity. Dr. J. L. Fahey, Dr. T. F. Dutcher, Dr. H. C. Goodman: Cell Nuclei and the Serum Gamma Macroglobulins.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY, 91, Dean Street, W.1
5.30 P.M. Dr. E. H. Larkin: Organic Dementia.
OSLER CLUB OF LONDON
8.15 P.M. (National Hospital.) Dr. Macdonald Critchley: History of the Hospital and the Square.
SOUTH-WEST LONDON MEDICAL SOCIETY
8.30 P.M. (Bolingbroke Hospital, S.W.11.) Dr. G. T. Stewart: Fats in Food, Blood, and Arteries.
LEEDS NEUROLOGICAL SCIENCES COLLOQUIUM
5.15 P.M. (General Infirmary at Leeds.) Prof. O. L. Zangwill: Asymmetry of Cerebral Hemisphere Function.

Wednesday, 16th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
4 P.M. Dr. J. A. Lee: Joseph Clover and the Contributions of Surgery to Anæsthesia. (Joseph Clover lecture.)
ROYAL SOCIETY OF MEDICINE
5 P.M. *Comparative Medicine.* Dr. Ruth Allcroft, Dr. Iain MacIntyre, Prof. A. Robertson: Magnesium Metabolism in Man and Animals.
8.15 P.M. *General Practice.* Dr. W. W. Fulton, Dr. Harvey Flack, Sir Frank Newsam: What is a Family Doctor?
ROYAL FREE HOSPITAL, Gray's Inn Road, W.C.1
5.15 P.M. Dr. B. E. C. Nordin: Metabolic Bone Disease.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. Arthur Tickner: The Biochemistry of Psoriasis.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Mr. D. S. M. Barlow: Pathology, Treatment, and Complications of Achalasia.
HARVEIAN SOCIETY OF LONDON, 11, Chandos Street, W.1
8.15 P.M. Prof. J. Waldenström (Lund): Gamma-globulin. (Harveian lecture.)

Thursday, 17th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P.M. Dr. A. E. Jones: Supervoltage X-ray Therapy of Intracranial Tumours. (Hunterian lecture.)
BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, W.1
8 P.M. Dr. Frank Ellis, Mr. R. E. Ellis, Dr. N. G. Trott, Dr. K. W. Taylor: Reduction of Radiation Hazards in the Use of Radium and Similar Sources.
WEST LONDON MEDICO-CHIRURGICAL SOCIETY, West London Hospital, W.6
8 P.M. Mr. P. D. Trevor-Roper: Influence of Eye Disease on Pictorial Art.

Friday, 18th

ROYAL SOCIETY OF MEDICINE
5.30 P.M. *Epidemiology & Preventive Medicine.* Dr. W. R. S. Doll, Dr. W. M. Court Brown: Studies on the Possible Effects of Low Doses of Radiation.
8.15 P.M. *Radiology.* Mr. Hedley Atkins, Mr. Murray Falconer: Relative Values of Adrenalectomy and Hypophysectomy on Advanced Carcinoma of the Breast. Mr. Gordon Ramsay: Interstitial Irradiation of the Pituitary. Dr. J. J. Stevenson: Localisation of Radioactive Implants with Image-intensification and Television.
POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M. Mr. R. G. Pulvertaft: Advances in Hand Surgery.
4 P.M. Dr. Fraser Roberts: Medical Genetics.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3.30 P.M. Dr. Norman Hulbert: Vertigo—Differential Diagnosis.